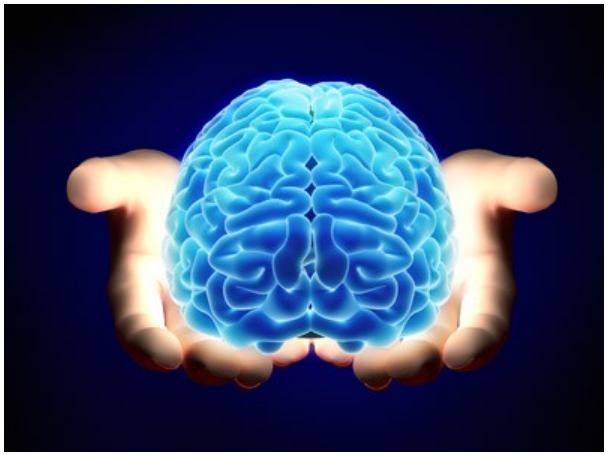
MASARYK UNIVERSITY
FACULTY OF MEDICINE

Neurosciences



Anna Malmström

Brno 2010/2011

Cytoskeletal components of neurons & their functions in regeneration

Cytoskeleton = serves for cell shape + movement of organelles / entire cell.

Components:

Intermediate filaments

10 nm

Exist diff types in diff. tissues.

Neurofilaments are the intermediate filam. in the neuron

Consist of neurofilament proteins:

NF-L
NF-M
NF-H

In neurodegenerative diseases these protein changes

Are most abundant of fibrillar elements in the neuron: It forms the core of the cytoskeleton

(forms core of cytoskeleton)

Microtubules

24 nm

Consist of 2 tubulin proteins (α + β-tubulin)

α-tubulin is considered to be the (+) end;
β-tubulin to be (-) end

In axon orientation of microtubules are:
(+) end directed externally!

Changes in lengths of microtubules are done by polymerization/depolymerization.

Inhibitor of polymerization:
Colchicin
Drugs fixing microtubules:
taxol.

Are narrow longitudinal tubes present in all neuronal processes. They maintain shape and also transport molecules such as neurotransmitters in vesicles from soma to axon terminals.

(Shape + transport)

Microfactin filaments

5-8 nm

Made of many G-actin monomers. Together, they organize a double-stranded helix. The polymer is called F-actin.

Inhibitor of actin polymerization:
cytochalasin-B

Inhibitor of actin depolymerization:
phallotoxins.

Present in high conc. as a mesh work beneath the membrane of axon. Actin is an imp. protein in neurodevelopment.

(up in axon)

Types of axoplasmatic transports, their functions in the intact neuron

Transport type	Speed	Mechanism	Material transported
Fast anterograde	400 mm/day	Saltatory movement along microtubules by the motor molecule Kinesin (ATP dependent)	• Mitochondria • Vesicles containing peptide & other neurotransmitters.
Fast retrograde	200 mm/day	Saltatory movement along microtubules by the motor molecule dynein (ATP dependent)	• Degraded vesicular membrane. • Absorbed materials ex toxins, viruses.
Slow anterograde	0,2-8 mm/day	Not clear	• Cytoskeletal elements ex. neurofilaments & microtubule subunits. • Soluble proteins of intermediary metabolism • Actin.

If the flow of materials from soma to distant axon terminus would function as simple diffusion their delivery would be far too slow to be of any practical use. Therefore cell use fast anterograde axoplasmatic transport:

Organells + vesicles + mitochondria + molecules attached to them (such as proteins, lipids, polysaccharides) move along microtubules with help of a motor protein called kinesin. It need ATP to function.
Kinesins always move toward the plus-end of microtubules = away from the soma.
Nervous system has many forms of kinesin that recognize and transport different cargo.

In fast retrograde axoplasmatic transport materials are brought from axon back to soma with help of a diff. motor protein called dynein = move toward minus-end

The loss of ATP-production causes fast axoplasmic transport in both directions to fail!

Slow axoplasmatic transport – is used by many proteins, including cytoskeletal proteins. The transport is anterograde. Motor proteins are involved, but mechanism is not very good understood.

s. 272 - Boron

Types of neuronal synapses and their characteristics by morphology & transmitters

- Electrical
- Chemical

} → se annan följa!

- Morphology & function → se bild annan följa!

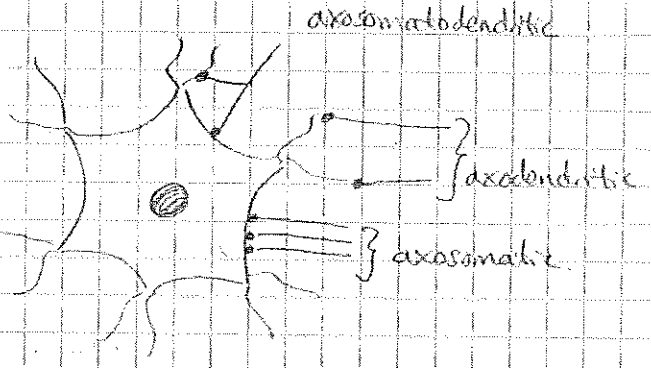
Transmitters:
Inhibitory
Excitatory

- acetylcholine
- noradrenaline
- dopamine
- serotonine
- GABA
- glycine
- glutamate

Classification of synapses

Central axes:

- axodendritic
- axosomatic
- axosomatodendritic



Peripheral axes:

- neuron + effector cell

Synapses are named as boutons on smooth muscle cells, cardiomyocytes & glandular cells.

motor end plates on skeletal muscle cells.

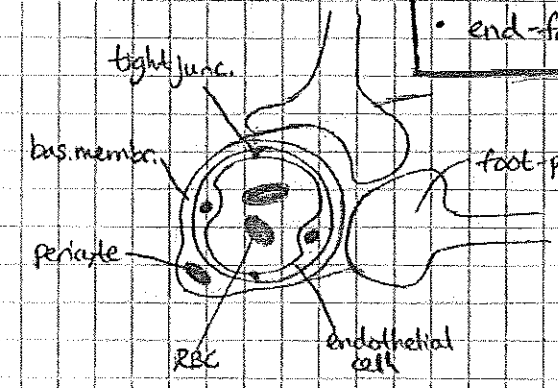
Structural basis for hematoencephalic barrier and its significance.

Blood-brain-barrier prevents some substances in blood from crossing the vessel walls in CNS and enter the ECS in brain.

A BBB is necessary because blood is not a suitable environment for neurons. Blood contains many substances and these substances can vary greatly in concentration depending on eg. diet, metabolism, illness, age...
Ex. after a protein-rich meal the conc. of AA ↑. Some AA act as neuro-transmitters within the brain. If these molecules could move freely from blood into brain they would activate receptors and disturb the normal neurotransmission.
So for brain to function normally, it must have a BBB.

BBB consist of:

- endothelial cells (joined by tight junctions which prevent molecules to escape from blood) (with no fenestrae)
- basement membrane
- pericytes (may be present in basement membr. They have supportive function)
- end-foot processes of astrocytes (they cover the capillaries)



BBB protects brain from common bacterial infections. However, if infection do occur in brain they are very serious + difficult to treat, because antibodies + antibiotics are too large to cross BBB. However, BBB becomes more permeable during inflammation, meaning some antibiotics can get across. Viruses pass BBB easily by attaching circulating immune cells.

Structures free of total hematoencephalic barrier; functional effect

Some areas of brain lack a BBB.
It means that substances in blood can pass into ECS in brain at these sites through gaps between the endothelial cells.

These small areas are called circumventricular organs, because they surround the ventricular system.

- Area postrema – chemoreceptor which stimulate vomiting if you've eaten a special drug etc.
- Organum subfornicale } – are chemoreceptors which regulates
- Organum subcommissurale } components in CSF.
- Organum vasculosum – at lamina terminalis. Here leakiness is important because ncl. suprachiasmaticus release hormones to capillaries here which acts as signals to temperature control centers that are involved in fever.
- Eminentia mediana – Here neurons (for hypothalamus) release hormones which go into the hypophyseal-portal-system of ant. hypophysis and inhibit/stimulate release of ant. hypophyseal hormones.
- Posterior hypophysis – Lack of BBB is imp. here because it allows hormones released by the hypothalamo-hypophyseal-system to enter the general circulation
- Pineal gland – secretes hormone melatonin directly into general circulation. The molecules of this hormone is too large to pass through BBB, therefore it doesn't have a BBB.

Why these areas lack BBB is because they are a part of a neuroendocrine control-system which maintain for example hormone levels.

These organs secrete different hormones, neurotransmitters and cytokines.
As a result of no BBB neurons located in these areas can directly sense the concentrations of various compounds (eg. hormones) in bloodstream without the need of specialized transport systems which move these substances across BBB.

Transport mechanisms through the hematoencephalic barrier

Things that easily cross BBB: gases such as O_2 & CO_2, drugs such as ethanol, caffeine, nicotine & heroin. And other small lipophilic molecules.

Things that don't cross BBB: bacteria, large molecules, lipophobic molecules eg. glue, AA, neurotransmitters

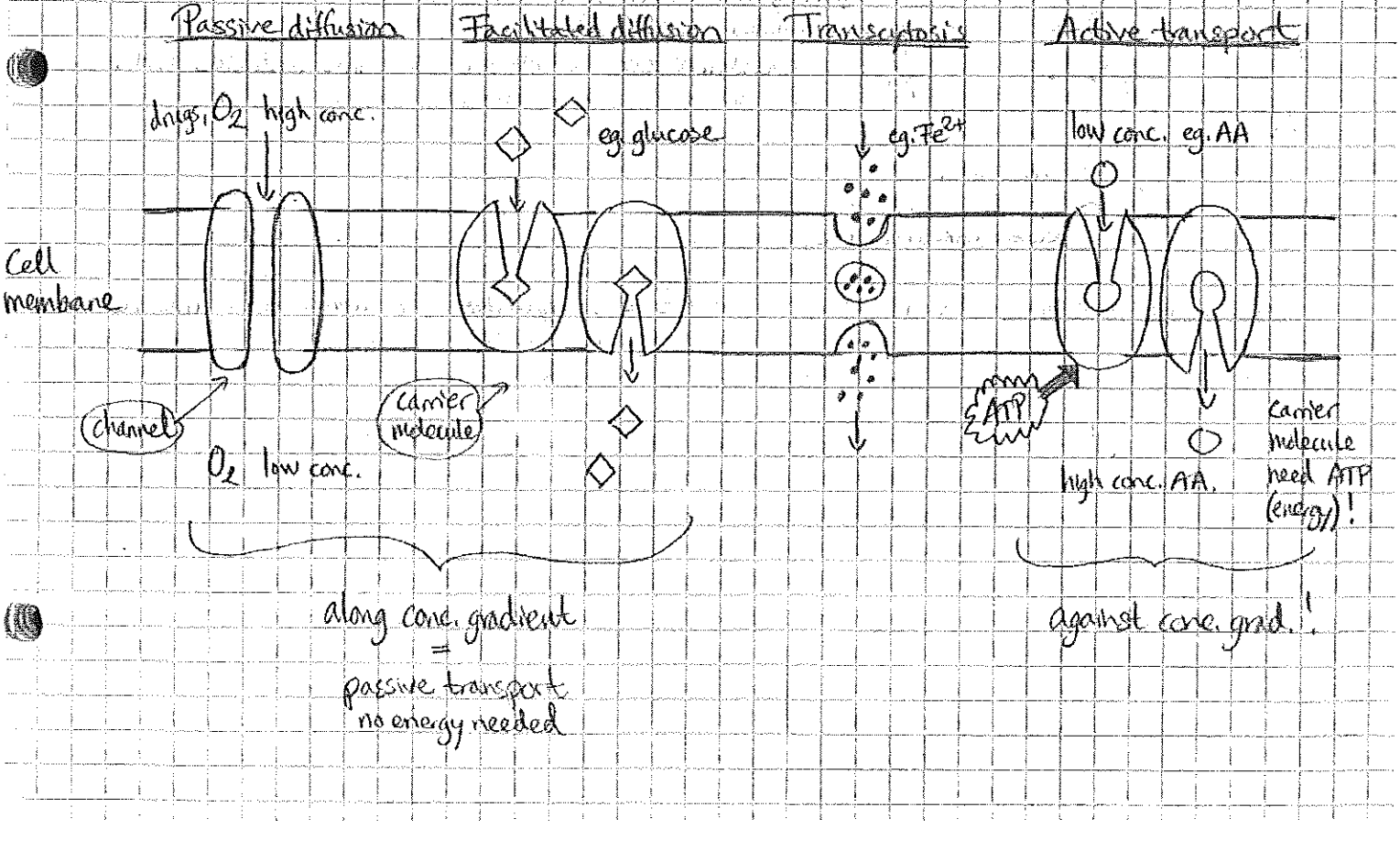
There are 4 basic mechanisms by which molecules can move across membranes: (passive transport)
- Simple diffusion = from high to low conc. Ex. O_2, CO_2, lipophilic substances.
- Facilitated diffusion = using a specific membrane protein carrier, no energy needed. Ex glucose
- Transcytosis = transport with help of coated vesicle. Ex. Fe-ions.
- Active transport = carrier protein + ATP. Ex aminoacids & K^+.

Movement of molecules btw cells = paracellular diffusion
Movement of molecules across cells = transcellular diffusion

Because of the tight junctions in BBB only transcellular diffusion is possible

The general rule for transcellular diffusion is:
"The higher the lipophilicity of a substance, the greater the diffusion into brain and the smaller molecule, the faster it diffuse". But in order for nourishment to reach brain lipid-soluble components must cross BBB. To achieve this transfer brain vessels have special carriers which transport them. In conclusion, BBB is crossed by:
1) Small, lipophilic molecules. Ex. O_2, CO_2, drugs. Use diffusion.
2) Water-soluble compounds that pass BBB by specific transporters. Ex. glucose, AA, neurotransmitters...

(2 major transporter groups! SLC superfamily, ABC transporters)



Formation and absorption of cerebrospinal fluid. Function of CSF.

CSF is a colorless, watery liquid that fills the ventricles of brain and forms a thin layer outside the brain + spinal cord in subarachnoid space.
It's secreted by choroid plexus in lat. ventricle → foramina interventriculares to 3rd → aqueduct of Sylvius to 4th → aperture of Luschkae + aperture of Magendie → subarachnoid space with cisternaes → granulationes and becomes absorbed into venous blood in sin.sag.sup. (special evaginations of arachnoidea into sinuses)

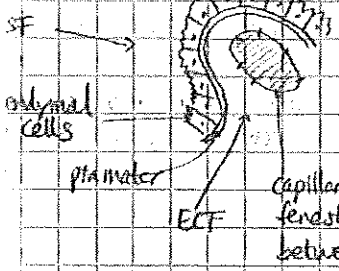
- An imp. function of CSF is to protect brain from mechanical injury, like a shock-absorbing cushion.
- Another imp function is that CSF makes the brain "lighter". The actual mass of brain is 1400 g, but when suspended in CSF its mass is less than 50 g. This has to do with the difference in gravity of brain tissue and CSF. Otherwise blood flow would be cut off.
- CSF also takes metabolic waste away from CNS through BBB.
- CSF also regulate the intracranial pressure. If press is too high ⇒ CSF ↓ ⇒ press ↓ o blood flow ↑ = prevention of brain ischemia (by increasing the absorption in gran. Not by ↓ formation)

Site of formation: Choroid plexuses = folds of pia mater and blood vessels, covered by ependymal cells which apical surface have microvilli and project into the ventricle.

Blood flow into plexues is 10x greater than cerebral blood flow. Symp + parasymp. nerves innervate each plexus. Symp. stimulation = inhibit CSF formation.
Capillaries inside plexuses are leaky and not inside BBB! But, the endothelial cells are still joined by tight junctions.

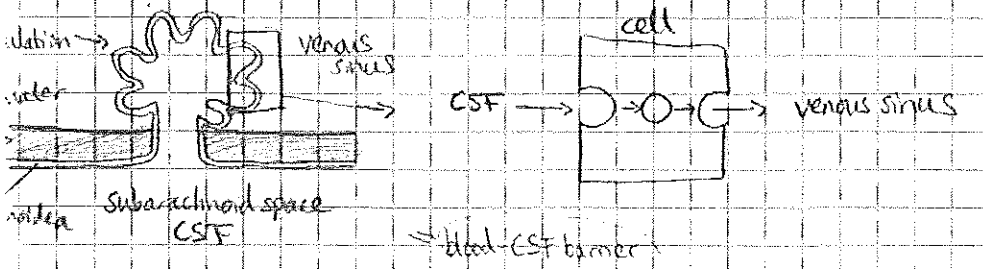
CSF production: 500 ml/day. Composition: ions, water, AA, proteins, glucose

CSF forms in 2 steps: 1) First, ultrafiltration of plasma occurs across fenestrated capillary wall into ECF
2) Then ependymal cells secrete the fluid into ventricles with help of diff. transport mechanisms.



Site of absorption: Arachnoid granulations = evaginations of arachnoid membrane through duramater into the lumen of venous sinuses.

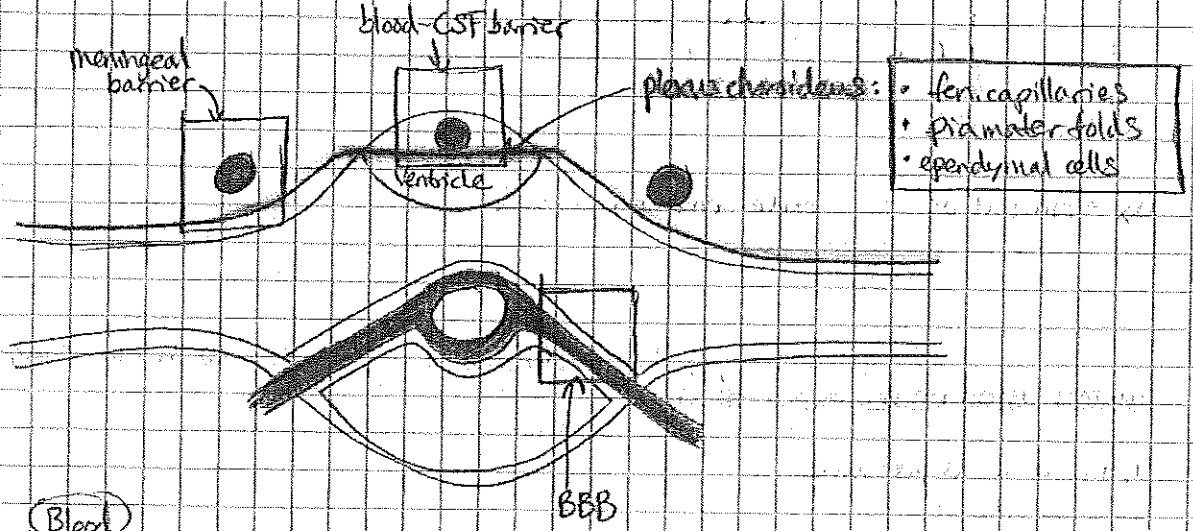
Fluid can move from subarachnoid space to venous sinus, but not the other way!
The absorption is believed to involve transcytosis = formation of giant fluid-containing vacuoles that cross from CSF side to blood side.



The CNS liquid compartments and their barriers

Barriers between liquids in CNS:
- Meningeal barrier
- Blood-brain-barrier (BBB)
- Blood-CSF barrier

Liquid compartments in CNS:
- Intracellular compartment (neurons + glia)
- Extracellular compartment (ca 20 nm wide between cells, ca 25-40 % of volume of brain)
- CSF
- Meningeal blood vessels in dura mater.



BBB (Blood | endothelial cells, basement membr., pericytes, end-foot processes astrocytes | Brain ECT)

choroid plexus cells + arachnoid membrane } **blood-CSF barrier**

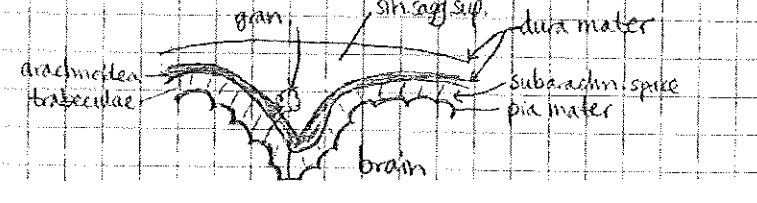
Unlike capillaries in BBB, choroid plexus has fenestrated capill. and no tight junctions.
The ep. cells in choroid plexus + cells in arachnoidea are linked by tight junctions.

Meningeal barrier:

Pia mater – delicate, highly vascularized c.t. layer.
Closely cover brain + spinal cord
Connected to arachnoidea by trabeculae.
→ subarachnoid space + cisternae = CSF

Arachnoidea – delicate, non-vascular c.t. membrane.
Form granulationes ⇒ project into sinuses, mainly sup. sagg.
→ subdural space

Dura mater – outer layer, dense c.t., vascularized by meningeal vessels.
Two layers in brain ⇒ separated → sinuses
⇒ together → falx cerebri etc.



Measuring of the cerebral blood flow

Normal blood flow to brain = 50 ml/100g brain tissue/min.
Brain weight 1500 g has a normal blood flow of 750 ml/min.
Even a small interruption of blood supply to CNS may result in serious neurological disturbances.

A blood flow of 25 ml/100 g tissue/min lead to damage of brain cells, called ischemic penumbra.
— " — 8 ml/100g tissue/min lead to an almost complete loss of neuronal function.
Within 10 sec. consciousness is lost in no blood flow at all.

Cerebral blood flow can be measured by determining the amount of nitrous oxide (N_2O) removed from the blood stream (Q_x) per unit time and dividing it by the difference between the concentration in the arterial blood (A_x) and in venous blood (V_x)

$$CBF = \frac{Q_x}{A_x - V_x}$$

Q_x = amount of nitrous oxide removed from blood
A_x = conc in arterial blood
V_x = " " venous "

Factors affecting cerebral blood flow:

1) Intracranial pressure
2) Blood viscosity
3) Mean venous pressure
4) Mean arterial pressure
5) Constriction and dilatation of cerebral arterioles.

Use Fick's principle.

Inject N_2O into a vein and its conc. is measured in arterial blood.

$$CBF = \frac{N_2O \text{ consumption (ml/min)}}{(\text{conc } N_2O \text{ in artery} - \text{conc } N_2O \text{ in vein})} = 750 \text{ ml/min.}$$

Blood flow in various parts of the brain / Regulation of cerebral circulation. Brain metabolism.

Blood supply to brain is derived from 2 arteries:
1) Internal carotid artery - the major source of blood.
2) a. vertebralis

These two systems of arteries anastomose at the base of the brain into the circle of Willis. If a stenosis is formed in one artery, the circle can provide an alternative flow.

Blood flow in various parts of brain is distributed according to local activity in the brain.
Blood flow is determined by a number of factors such as viscosity of blood, how dilate the vessels are, blood pressure and intracranial pressure.
Cerebral blood vessels are able to change the flow of blood by altering their diameter in a process called autoregulation.

They constrict if blood pressure is ↑, and dilate when BP ↓.
They also constrict or dilate in response to chemical concentrations, ex they dilate in response to ↑ CO_2.

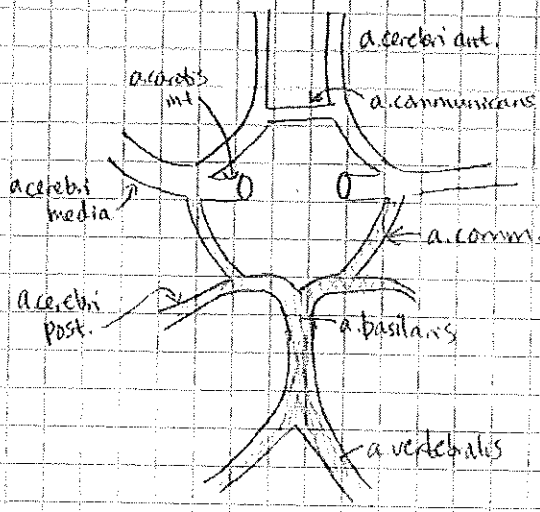
Myogenic control = ↑BP lead to constr.
↓BP lead to dil.

Metabolic control = a local ↑ in brain metabolism lowers pO_2 and raise pCO_2.
↑CO_2 lowers the pH and this triggers vasodilatation.
More blood → more glue.

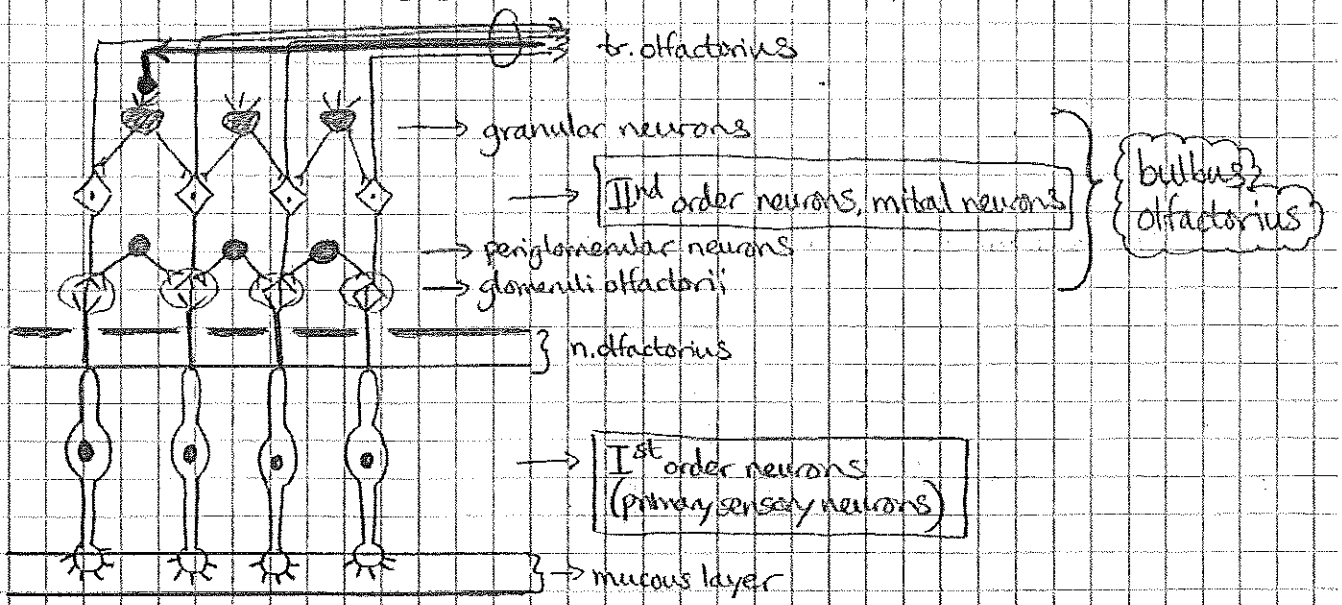
Neural control = Sympathetic nerve terminals release norepinephrine which cause vasoconstr.
Parasymp. nerves cause vasodil.

Brain receives ca 15% of cardiac output and consumes ca 21% of total O_2.
Each day brain oxidizes 100 g glue.

If blood flow is restricted for some seconds it can lead to irreversible damages.



The neurons and their connections in the olfactory bulb



Dendrites of sensory neurons are enlarged & embedded in the mucosa of regio olfactoria nasi, yellow colour in roof of nasal cavity.
Axons run through cribriform plate, they constitute n. olfactorius.

Axons terminate on IInd order neurons called mitral neurons.
The synapse btw Ist & IInd are enlarged and called glomeruli olfactorii.

In the level of this synaps we have some additional neurons, which can influence the signal in horizontal plane, called periglomerular neurons.

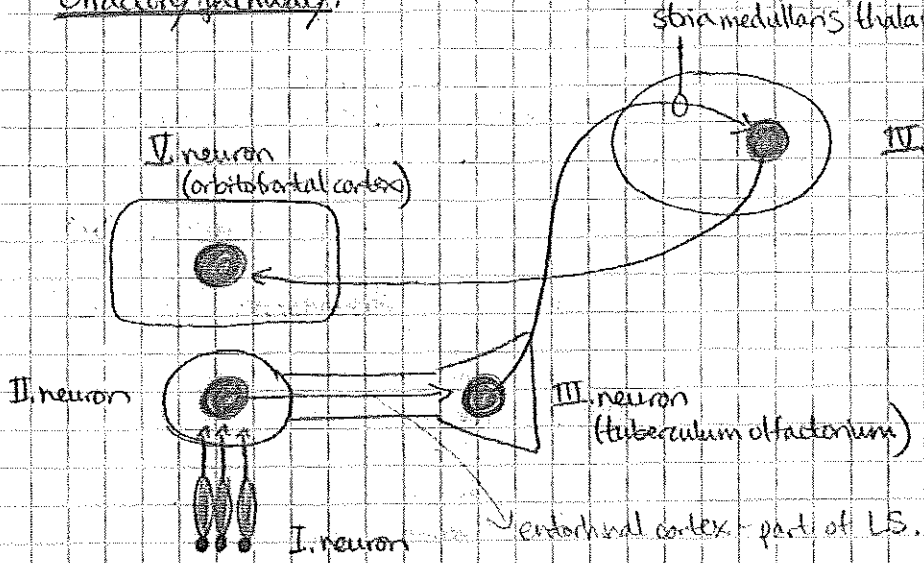
In the level of mitral neurons we have another additional neurons, called granular neurons. They also influence the signal in horizontal plane.

Axons of IInd order neurons constitute tr. olfactorius.
This tract also contains axons from mitral neurons from opposite side (red)
These axons terminate on granular cells and are important for orientation of where in the space the smell origin.

Dogs have very well developed bulbus olf.!

Pathway for conscious sense of smell

Olfactory pathway:



Axons in tr. olfactorius go to IIIrd order neurons in olfactory triangle which constitute a small hillock called tuberculum olfactorium.
Their axons continue to thalamus through stria medullaris thalami (s. 361.13 B) into nd. medialis dorsalis thalami. There we have IV order neurons.
Their axons project into olfactory cortex which is the orbitofrontal cortex (on inferior surface of brain lying on the orbital plate).
In this cortex lies Vth order neurons which analyze the taste.

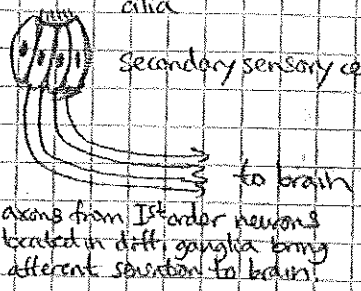
There is also an additional pathway for taste:
The signals from tr. olfactorius will go into pyriform and entorhinal cortex first and then sent to orbitofrontal cortex.

These cortexes are parts of limbic system and therefore important in our behavior when we smell. Ex. if we smell something bad we want to move away from the smell...

Taste buds and their innervation

Tastebuds contain secondary sensory cells derived from ep cells of mucous membrane.
Inside taste pore we have cilia from secondary sensory cells.
The sensory cells are innervated by dendrites of Ist order neurons.

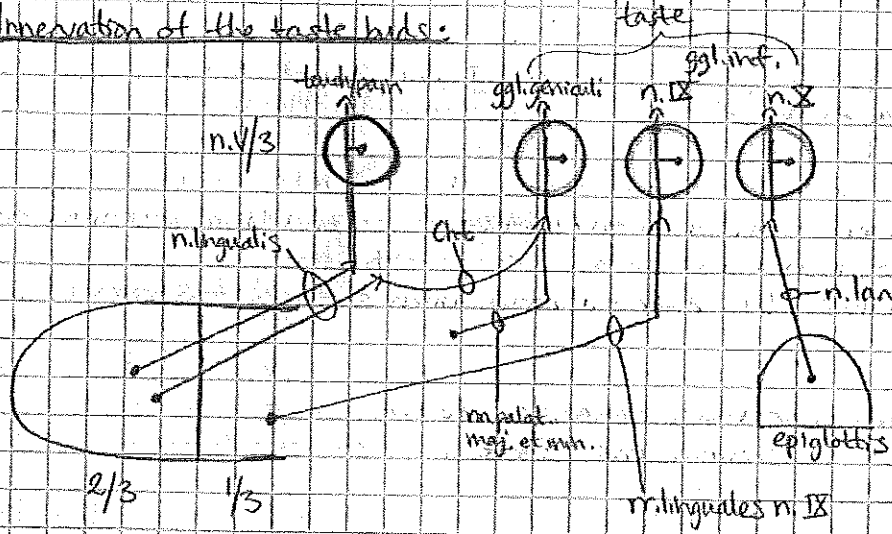
Tastebud:



Located in 3 types of papillae ⇒
- circumvallatae – V
- foliate – ///
- fungiformis – S

5 tastes: bitter, salty, sweet, umami, sour

Innervation of the taste buds:



Pseudounipolar neurons from ggl. trigeminale senses with their peripheral axons touch, pain etc. from ant. 2/3 of tongue. Axons are located in n. lingualis.

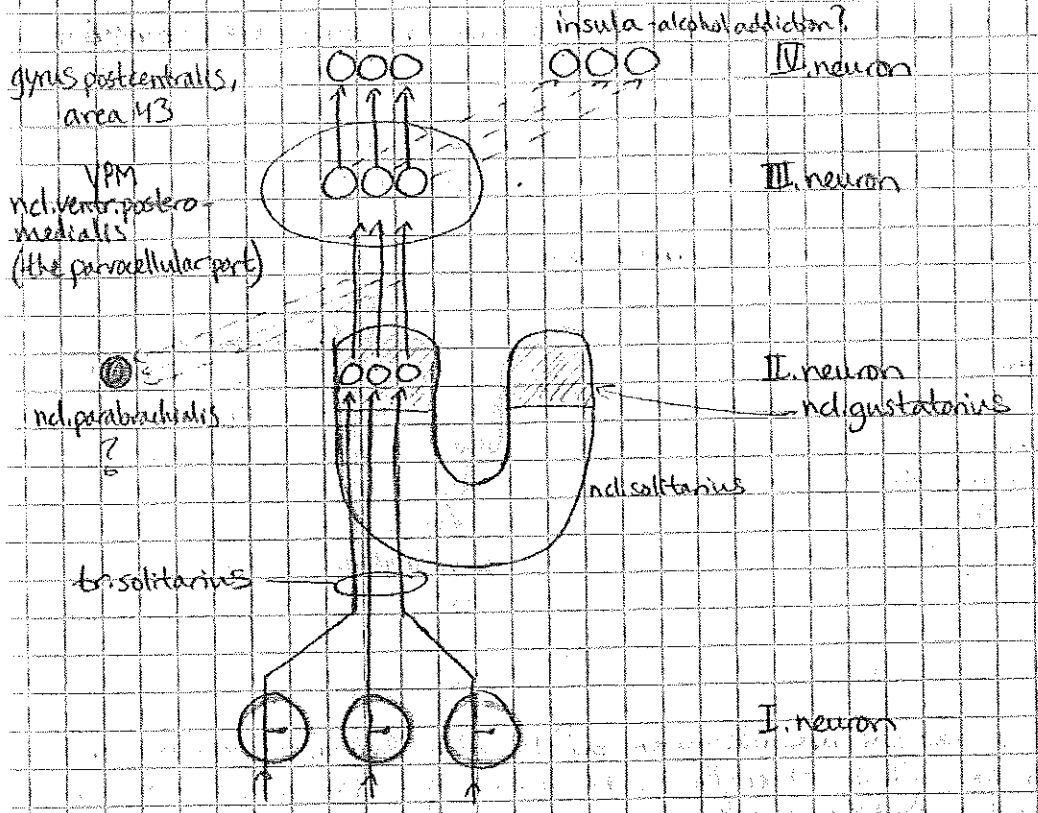
The tastebuds on ant 2/3 are however innervated by peripheral axons from pseudounipol. neurons located in ggl. geniculi. Axons travel in n. lingualis & chorda tympani + n. VII.
n. palatinus maj. et min. convey taste signals to ggl. geniculi from tastebuds on palatum.

Tastebuds on post 1/3 are innervated by peripheral axons from pseudounipol neurons in ggl. inferius of n. glossopharyngeus. Axons travel in rr. linguales.

Tastebuds on epiglottis are innervated by peripheral axons from pseud. neurons in ggl. inferius of n. vagus. Axons travel in n. laryngeus sup.

The proximal branches of these 3 taste pseudounipolar neurons end on nucl. solitarius.

Pathway that convey taste information to the upper structures of CNS



The pseudounipolar neurons in the 3 "taste ganglia" will end their proximal branch on ncl. solitarius, in ncl. gustatorius.
Ncl. solitarius is divided into different compartments. Ncl. gustatorius to one compartment.

II order neurons ends on III neurons on ncl. ventralis postero-medialis in thalamus. These neurons then project the signal to IV order neurons in cortex of gyrus postcentralis, it's the primary taste cortex.

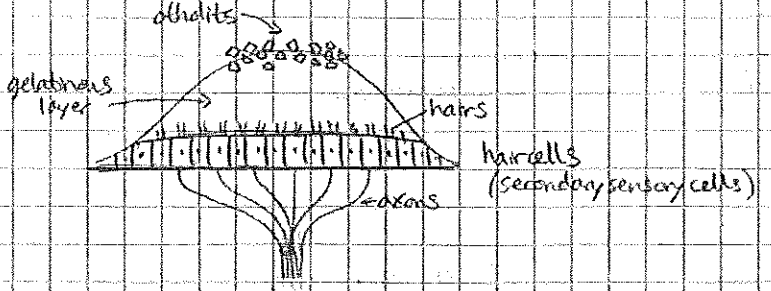
There is a secondary taste cortex = cortex in insula. We know that because if you're addicted to alcohol and get a stroke in insula, you'll stop drinking. So this cortex is strongly related to taste.

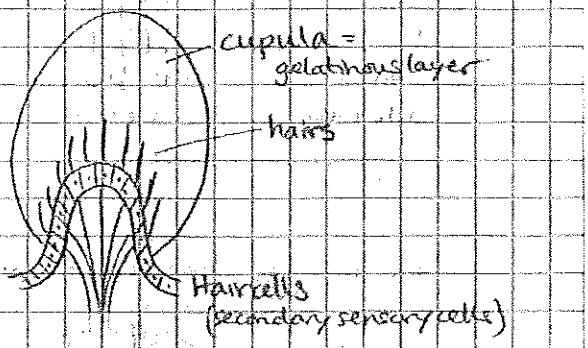
The vestibular pathways, scheme & its description

Vestibular system ⇒ sensation of our position (of head) in 3-D-space, located in inner ear.
When we close our eyes our proprioception is a combination of vestibular system + tonus sensation in muscles!

Linear acceleration: • macula utriculi – horizontal position
• macula sacculi – vertical position

Angular acceleration: – cristae ampullares (3 st)





Secondary sensory cells (haircells) are innervated by I st order neurons present in vestibular ganglion (s. 409. A. 3). Their axons join axons from spiral ganglion of cochlea and together they form n. vestibulocochlearis (VIII).

II nd order neurons for vestibular system are located in ncll. vestibulares.
Ncll. vestibulares are divided into:
- superior (Bechterev)
- inferior (Roller)
- lateral (Deiter)
- medial (Schwalbe)

These ncll. have connections with subcortical structures (such as spinal cord, brainstem and cerebellum) to coordinate our movements, without sending signal to be analyzed by cortex cerebri first!

Connections with spinal cord:

Deiters nucleus – tr. vestibulospinalis lat. → exist in all spinal chord levels, mediate signals for maintainance of muscle tonus of back muscles → for upright position!

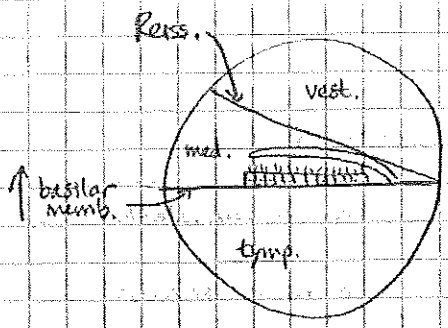
Schwalbes nucleus – tr. vestibulospinalis med → ends on motor neurons only in cervical + upper thoracic segments. Involved in coordination of position of head and to keep it at balance.

Connections with brainstem:
Through fasciculus longitudinalis med (FLM) ncll. vestibulares sends signals to ncll. orig. of n. III, IV and VI and also to Cajals & Darkschewitsch nuclei for coordination of movements of eyes and head. ⇒ (see § pathway f. vestibulo-ocular reflex!)

Connections with cerebellum:
Tr. vestibulocerebellaris = signals from ncll. vestibulares (sup, int, med) through pedunculus cerebell. inf. to pars flocculonodularis. And from here in tr. cerebellospinalis signals go in axons to motorneurons for trunk muscles for maintainance of balance.
(⇒ see q. connections of vestibular cerebellum!)

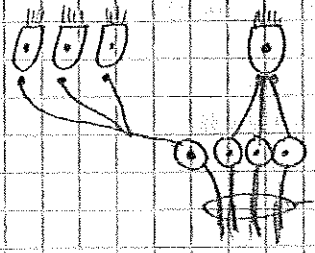
The pathways for hearing, scheme and its description

Hair cells are secondary sensory cells located inside cochlear duct. Duct divides cochlear canal into 3 spaces:
- Scala tympani - perilymph
- Scala media - endolymphatic space
- Scala vestibuli - perilymph



Scala media appears in transverse section as a triangular space. It has 3 walls:
- Vestibular membrane (Reissner's membr.)
- Tympanic floor with basilar membrane where the hair cells are located + covered by tectorial membrane.
- Lateral wall

Hair cells are innervated by dendrites of Ist order neurons located in spiral ganglion. Axons of spiral ganglion neurons then constitute n. cochlearis which combine with n. vestibularis to n. VIII.
Inner hair cells of organ of Corti = 1 row ⇒ innervated by many axons.
Outer hair cells — " — = 3-5 rows ⇔ — " — by collaterals of one dendrite

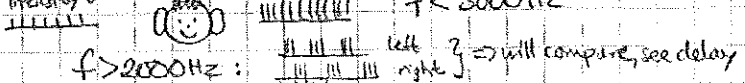


When basilar membrane shift ↑ due to waves in perilymph, hairs change position against tectorial membrane ⇒ AP arises
Signal is sent to IInd neuron.

IInd order neurons are located in ncl. cochlearis ventralis and ncl. cochlearis dorsalis.
In ncl. cochlearis ventr. - neurons receive signals about intensity of sound and of the direction/source of sound. These IInd order neurons send signals to superior olive nucleus (IIIrd) which then transmit the signal into lat. lemniscus to inf. colliculus.
However, some fibers from sup. olive will cross midline and terminate on trapezoid body (a mix of white + gray matter) and continue to sup. olive on opposite side.
Because of this second pathway it is possible to distinguish from where the sound came from, because neurons in trapezoid body inhibit the output of the neurons on the contralateral side and a difference of signal can be seen on both sides.

In ncl. cochlearis dors. - some other Ist order neurons terminate on IInd neurons. These signals are about the pitch of the tone. Some axons from these IInd neurons will go to coll. inf. on same side, some to coll. inf. on contralateral side. (IVth)

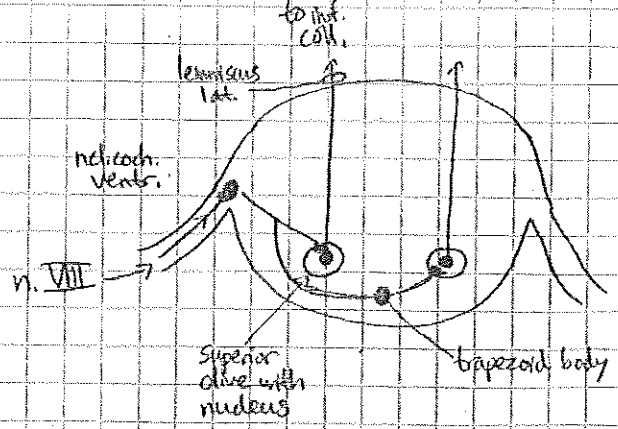
In ncl. cochlearis dors. neurons have tonotopic arrangement = arranged according to frequency level. Some analyze high freq., some low freq.



Localization of sound in space

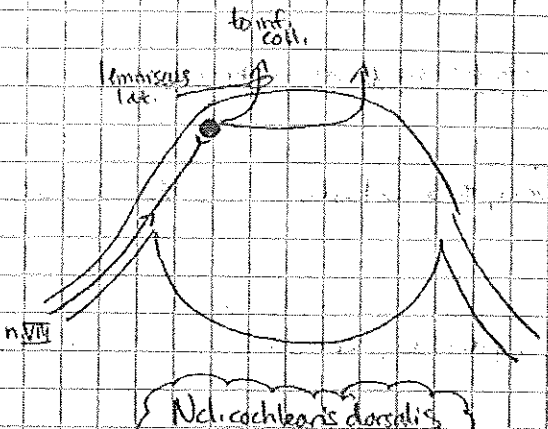
Or:
If frequency < 3000 Hz we localize the sound by comparing the sound waves received by each ear. The signals will be delayed in one ear.

If frequency > 2000 Hz we localize the sound by comparing the intensity of it. The intensity will be higher in one ear than in the other.



Ncl. cochlearis ventralis

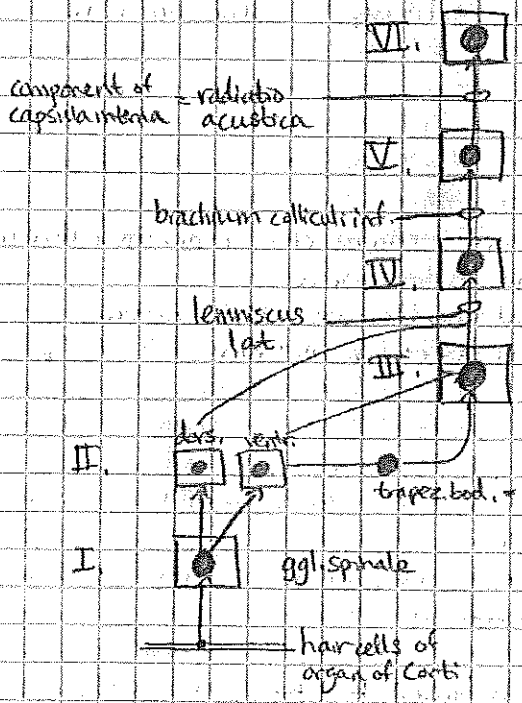
Intensity + direction of sound



Ncl. cochlearis dorsalis

Pitch of tone

Auditory pathway



Before ncl. corp. gen. med. some axons from contralateral ncl. collic. inf. pass to it in brachium coll. inf.

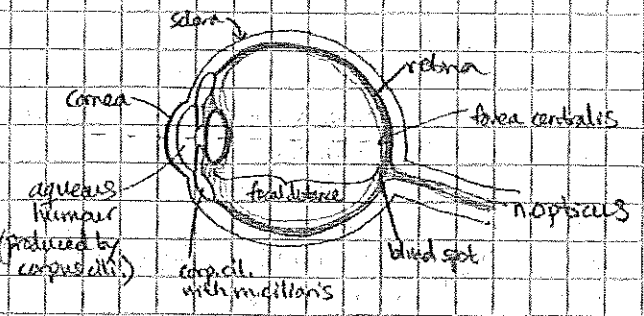
Descendent auditory pathways:

Afferent signals from outside can be modulated by cortex, exs. suppress extreme inputs. This is the mechanism when the sound around you is reduced because you focus to speak to one person on a loud party etc.

Optical system of the eye

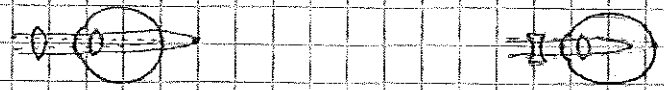
The eyeball is made up of:
- a wall, has 3 layers:
  - sclera + cornea
  - choroidea with corpus ciliare + iris with pupil
  - retina
- a content: aqueous humour + lens + corpus vitreum

Before forming an image on retina, the ray of light must pass through 4 optical media = cornea + aqueous humour + lens + corpus vitreum.



This optical system automatically focus the light on retina so that we can see a picture.
The automatic focusing of optical system is made possible by accomodation.
Optical power in whole eye = 60 diopters.
1 diopters = focal distance is 1 m.
60 diopters = focal distance is 16,6 mm.

Accomodation = the curvature of the lens is changed with help of m. ciliaris depending on the distance of the object we observe. Lens become thicker: +15 diopters.
The eye has two basic fixation points: the remote point = can be seen sharply without accomodation, the near point = can be seen sharply with maximum accomodation.
For children near point ≈ 9 cm away from eye, but the older we get the distance grow and in 80 years near point ≈ 80 cm, because flexibility of lens ↓. That's why old people read newspaper at distance. When distance exceeds 0,25 m a condition called presbyopia arises. Individual can't focus an object closer than 0,25 m. The focal point has shifted behind the eye and we must correct it with a biconvex lens ◊ which focus light on macula densa again.



presbyopia or farsightedness — nearsightedness

In young people:

Hyperopia = farsightedness is caused by a too short eye bulb so that focal point lies behind eye. Correction is same as for presbyopia.

Myopia = nearsightedness too long eye bulb, focal point lies infront of retina.
Correction: biconcave lens ⧓.

Astigmatism = the refractive surfaces don't have a symetrical shape ⇒ the focus is not a point. If astigmatism exceeds 0,5 D get blurred vision.
Simple astigmatism - one focal line on retina, the other one eiter infront or behind.
Compound - " - | - both focal lines lies infront or behind.
Mixed — " — | - one infront, one behind.

Convergence of axes + kalla vändögt

Reaction of pupil of light ⟹ If big = mydriasis. If small = miosis.

In accomodation pupil is small (miosis) because it's easier to concentrate the light on retina, but on the other hand we don't get so much light into eye.

Photopic and scotopic vision

The cones provide for vision under high intensities of light. They enable us to see details of shape and colour. They take over during adaptation to light. This adaptation is fast, it takes ca 20-60 seconds.
The vision of an eye adjusted to light is called photopic.

The rods provide for non-colour vision and become active at very low intensities of light. They play a role during adaptation to dark. This adaptation is slower, it takes ca 40-60 seconds to reach maximum adaptation.
The vision of an eye adapted to dark is called scotopic.

Transduction of light signal in photoreceptors

The photoreceptors contain visual pigments of a protein nature (rods - red rhodopsin, cones - violet iodopsin). The pigments are decomposed by the action of light, and it's the product of the decomposition that excite the receptors.

Ex. rhodopsin consists of retinal and opsin. Retinal is an aldehyde of vit. A and opsin is a protein carrier. When rhodopsin absorbs light retinal is transformed from cis-retinal to trans-retinal conformation. Cis-retinal can only exist in dark.
If trans-retinal is in contact with its protein carrier (opsin) it will return to cis-retinal in the dark. However, if retinal is separated from opsin, re-synthesis of rhodopsin from vit. A is necessary. If deficiency of vit. A adaptation to dark is bad = night blindness.
If you walk from outside into a dark room it will take a while before you'll adapt your vision to darkness. This is because rhodopsin must be regenerated from vit. A again.

The trans-retinal will trigger some changes in opsin that will cause it to change into metarhodopsin II, which will activate an attached molecule called transducin.
Transducin will cause activation of phosphodiesterase which will hydrolyse cGMP. In dark cGMP is synthesized within cytoplasm of photoreceptor. When phosphodiest. hydrolyze it, conc. of cGMP will ↓. cGMP normally keep Na^+ & Ca^{2+} ion channels open, but now channels will be closed!
Membrane will be hyperpolarized.

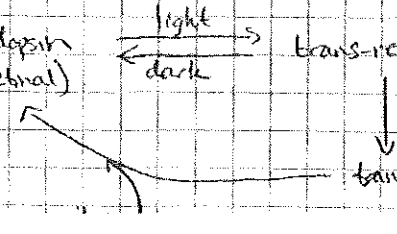
Trans-retinal and opsin separates in a process called bleaching, because they change colour when separate. Trans-retinal becomes retinol (vit. A) which becomes cis-retinal.

> In bright sunlight, rods become ineffective because most of their rhodopsin remains inactivated, or bleached. When return to darkness rods slowly regenerates rhodopsin and becomes sensitive once again.

Hyperpolarization:

In dark: membrane of outer segment is permeable for Na^+ and inner segment is permeabl. to K^+. The membrane of both segments are maintained in a depolarized state.
When light: outer segment membrane loose permeability for Na^+ & Ca^{2+}. The result is an increase in membrane potential ⇒ hyperpolarization. This hyperpol induces electrical phenomena in the other nerve cells of retina as well.

The receptor potential increases with increasing intensity of light stimulus up to a certain value.

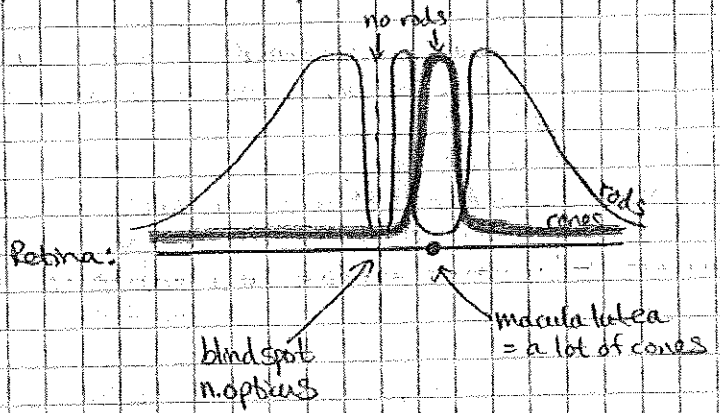


Photoreceptors - their function and retinal distribution

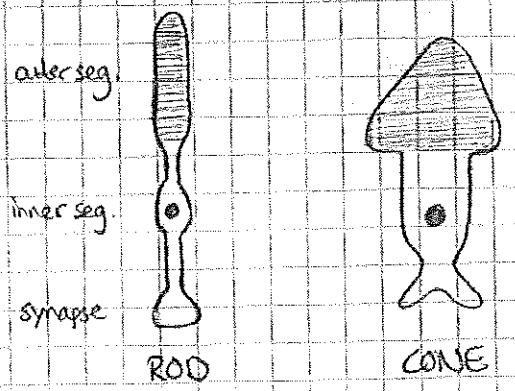
The light-sensitive elements (= photoreceptors) of the retina are called <u>rods</u> and <u>cones</u>.
Only about 10% of the light traveled into eye can stimulate the photoreceptors, 90% of the light is reflected or absorbed before reaching the receptors.

- Rods = synthesize rhodopsin = 120 millions = night vision.
- Cones = synthesize iodopsin = 6 millions = colour vision.

The maximum concentration of cones is in macula lutea (yellow spot), this is where vision is sharpest. It's a shallow depression in the retina at post. pole of eye.
The other layers of retina are heavily reduced at this site so macula lutea only consist of a layer of cones and the pigmented layer.
From macula towards periphery the cones decreases.
The maximum density of rods is within a circle about 20° from macula lutea. Their number decreases towards macula and periphery.
The blind spot don't contain any photoreceptors because this is the site where the n.opticus emerges.



Both types of photoreceptors are bipolar and consist of two <u>segments</u>: <u>outer segment</u> (in contact with pigment ep.) and <u>inner segment</u> (contain nucleus & mitochondria).
The inner segment is terminated by a spherical or cylindrical swelling where the synaptic connection to the bipolar cells are.
The outer segment in cones contains <u>invaginations</u> with <u>visual pigment</u> and in rods the outer seg. contain many <u>piled up discs</u> which contain visual pigment.



We have 1/2 millions fibers in n.opticus
It means that rods/cones are connected to many cells and that is called <u>convergence</u>.
More than one photoreceptor cell are connected to a single bipolar cell. Several bipolar cells transmitt info to a single ganglion cell, which carry info along its axons in n.opticus to brain.
The convergence is much more in rods than cones.
In primary visual cortex there are about 1000 neurons, so in this case we speak about <u>divergence</u>.

Mechanisms of color vision

Colour perception is the function of the cones. The mechanism of how we perceive colours has not been definitively resolved but there is a theory called trichromatic theory which assumes that retina contains 3 types of cones with different spectral sensitivity.
A stimulation of only one type results in the sensation of the relevant basic colour.
An even stimulation of all the 3 types of cones stimulate sensation of colour white.
An uneven stimulation results in a sensation of mixed colours.

The 3 cones are called: L-cone (565 nm red (long)), M-cone (535 nm green (middle)) and S-cone (440 nm blue (small)). Each of them contain a diff. pigment that is maximally sensitive to one of the primary colors: red, green, blue.

Color is mediated by ganglion cells, they can take away or add inputs from the diff. types of cones. Processing of the signals also occur in lateral geniculate nucleus and from here the signals can move in 3 pathways:

- Red/green pathway (L-M) – it signals the difference between L- and M-cone responses. This pathway project to primary visual cortex.
- Blue/yellow pathway (S-(L+M)) – that signals difference between S-cone and the sum of L- and M-cone responses.
- Luminance pathway (L+M) – it signals the sum of L- and M-cone responses.

All these 3 pathways project to primary visual cortex. (V_1)
Visual cortex can project the signals further to color vision areas. (V_8)

↳ See # (Visual cortex!) → Längre fram!

Color blindness

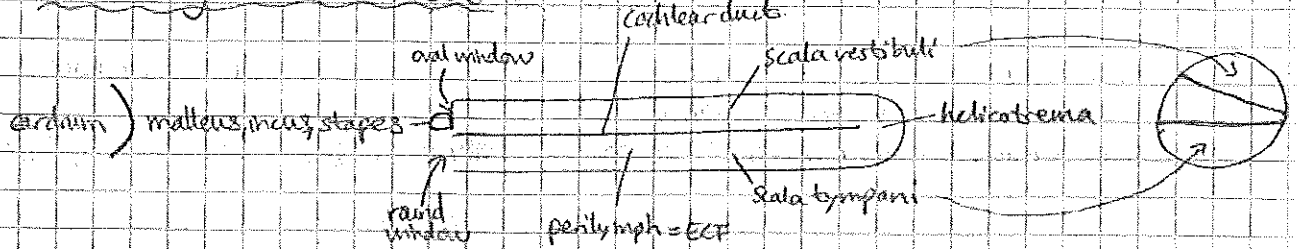
trichromatic = individual with normal colour sense, have all 3 systems for color vision.
monochromatic = a complete loss of colour sense, see only shade-white, like a grey photograph.
dichromatic = retina lacks a mechanism for perceiving one of the 3 basic colours.

↳ The loss of ability to see red = protanopia
— " — green = deuteranopia
— " — blue = tritanopia

The colour sense examination is based on the principle that objects or symbols of different colours, but with same brightness, seem to be of the same colour to the colour-blind person.
Pseudoisochromatic charts are used. A dichromatic person will not recognize the letter or figure.

Function of tympanic membrane & middle ear ossicles

Traveling wave in cochlea



Sound waves move eardrum which make the bones in middle ear to move.
The bones serves as amplifiers. The area of eardrum is bigger than oval window, therefore the pressure on oval window is greater. The pressure is increased almost 20X.
The bones have also a damping effect, they will decrease the "after-oscillations" of the membranes and perilymph. When a system is returned to equilibrium as quickly as possible without "after-oscillations" it is said to be "critically damped", this is what happens here.

Cochlea resembles a snail's shell, it's about 35 mm long. The basis of cochlea communicate with middle ear by two windows. Cochlea is divided into 2 compartments by cochlear duct. In crossection it looks like a triangle, filled with endolymph. Scala tym + vest = perilymph.

The acoustic oscillations are transmitted through oval window to perilymph. The basilar membrane start to vibrate and its movements cause the hair cells to be excited by the tectorial membrane. The basement membrane will not vibrate everywhere, only in some areas. The location of these areas is dependent on the frequency of the sound waves.

Speed of sound: 340 m/s
We can hear waves btw: 16000-20000 Hz. Over = ultrasound. Under = infrasound.
We have ca: 25 000 hair cells.
We can hear: 0-100 dB normal. If higher = pain.

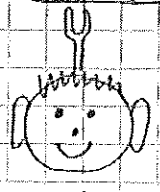
Middle ear has also a protective function against damage by strong impulses:
mm. tensor tympani + stapedius => decrease amplification of ear bones when sound is too high.

Sound waves = oscillations of the pressure of air, can reach the receptors in inner ear in 3 ways:
air conduction = use the auditory ossicles as described above.
bone conduction = acoustic vibrations travel through bones of skull.
conduction through round window = sound waves are transmitted to perilymph by vibrating its membrane.

Two types of hearing disorders:
conduction deafness = something is wrong with bones, eardrum etc.
nervous deafness = something wrong with haircells or nerves or brain.

To check which type of deafness, 3 ways how to examine:

Weber test



Put a tuning fork on head.
If don't know from where the sound comes = ears are ok.
If sound can be heard by one ear there is a problem with this ear.

Rhinné test

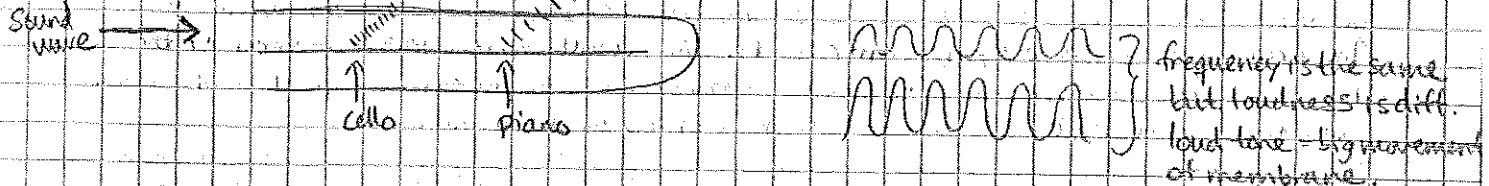
Put fork at proc. mast. and patient must say when sound dissapears. As soon as sound dissapear put fork infront of ear, a normal ear will hear the sound for ca 45 sek more, if don't hear = conduction deafness

Schwabach test

If put fork infront of ear and hear nothing and then on proc. mast. and can hear it's nervous deafness.
Can hear through bone but not through ear.

Loudness = corresponds to the amplitude of the sound (or the pressure changes in air). Loudness is a threshold quantity, it means that a specific minimum intensity of the acoustic stimulus is needed to stimulate the organ of hearing. This threshold intensity is different for each frequency.
Loudness depends on how many AP which are formed. Whisper = not so many AP, = silent
Street noise = many AP, = loud

Pitch = depends on the frequency of liquid. f activates different areas of membrane making it possible for us to distinguish the pitch of the tone. The pitch is determined by the location with maximum stimulation.



Usually low tones at apex of cochlea and high tones at the base.

Functions of inner and outer cochlear hair cells

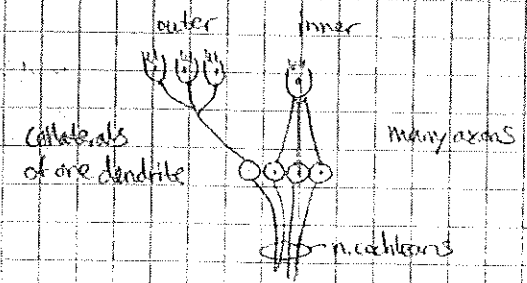
The sensory receptors (hair cells) located in the basal portion of the basilar membrane respond to high frequencies of sound, while hair cells located in the apical aspect of membrane respond to low frequencies. This is called tonotopic distribution.

1. A high frequency wave travels only a short distance and then dies out.
2. A medium frequency wave travels half and dies out.
3. A low frequency wave travels the entire distance.

The hair cells transform the vibrational energy into electrical signals
Located in inner ear in cochlea.
There are 2 types:
- Outer hair cells = lie in 3-5 rows. Are supported by outer phalangeal cells.
- Inner " " = lie only in 1 row " " " inner " "

Apices of hair cells are provided with stereocilia.
- W-shaped in outer cells = the tip of them are embedded in tectorial membr.
- Linear-shaped in inner cells.

The inner hair cells are the primary sensory cells which generate the AP in auditory nerve.



Transduction of an auditory signal

Perilymph & endolymph are electrolytes with diff. ionic composition.
There is a resting potential difference of +85 mV between the two environments.

Perilymph:	$Na^+ = 150$	Endolymph:	$Na^+ = 1$	Endolymph is produced by
ECF	$K^+ = 3$	ICF	$K^+ = 150$	stria vascularis
	$Cl^- = 130$		$Cl^- = 130$	

Air pressure waves cause tymp membr. to vibrate, resulting oscillatory movements of stapes against oval window. This result in pressure waves to form in perilymph present in scala tymp. & vestibuli. This cause vibration of the basilar membrane.
The tips of stereocilia of the outer hair cells are embedded in tectorial membrane, and the bodies of hair cells rests on basilar membrane. An upward displacement of basilar membr. result in lateral displacement of stereocilia.
This cause an influx of K^+ through their cell membrane. The hair cells became depolarized. This cause voltage-sensitive Ca^{2+} channels to open and Ca^{2+} goes into cell. This cause a release of neurotransmitter that elicits an AP in the afferent nerve terminal at the base of the hair cell.

A downward displacement of basilar membr. cause a medial displacement of stereocilia. This result in a hyperpolarization of hair cells and cause voltage-sensitive K^+ channels to open and K^+ goes out of cells.

Responses to angular and linear acceleration

When head starts to rotate in any direction (angular acceleration) the endolymph in semicircular canals wants to remain stationary (because of its inertia. Inertia means that an resting object will remain in rest until a force causes it to move) while the semicircular canals move.
This cause a fluid flow in the direction opposite the head rotation.
Hair cells in cupulla bends & send signals.
When rotation stops, endolymph continues to rotate while semicircular ducts stops.
It takes a few secands before endolymph stays and cupulla can return to its resting position.

Linear acceleration is detected by macula in utricule & sacculae.
When bend head forward or backward the cilia of hair cells are bend by otholits and signals are sent to CNS.

Somatosensory pathways from skin of body and extremities, scheme and its description

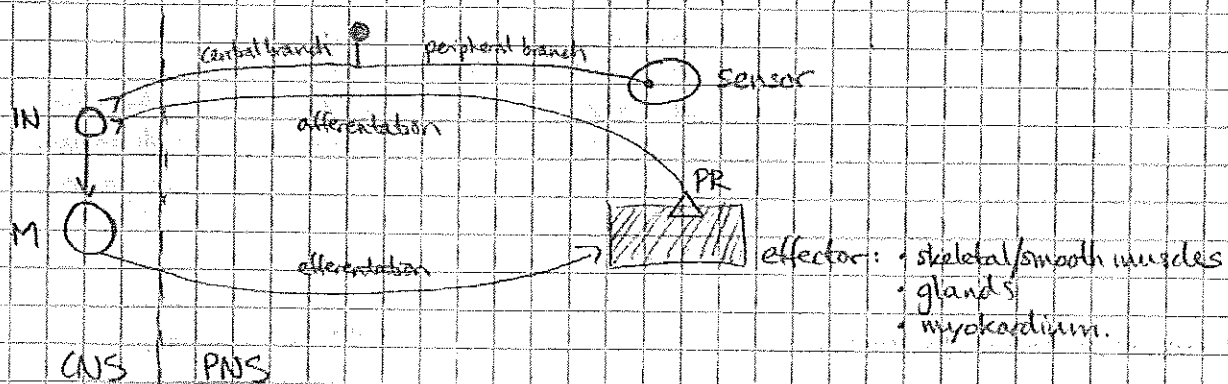
Somatosensory system = a sensory system which contains receptors and processing centres for our body to sense modalities such as touch, temp., proprioception (body position) and nociception (pain). The receptors covers skin, mucosa, muscles, bones and joints and internal organs.

There are diff. types of sensors:
General sensors ⇒ thermosensors
mechanosensors = touch & quality of things we touch
nociseneors = sense damage of tissue or when cold/hot becomes painful
(discriminative) tactile sensors = on fingertips
proprioseneors = present inside effectors.
somatoviseral sensors = present in wall of viscera.
Special sensors ⇒ components of sensory organs, ex. rods/cones in retina.

(touch/position)
Tactile sensation = is info about where the touch is and it distinguish two points from each other. We have high quality of tactile sensation on fingertips, but not so high on back. By means of tactile sensation it's possible to distinguish surfaces. Stereognosia = when we're able to recognize an object/surface when we close our eyes.

Proprioception = important for CNS to recieve info about stage of effector and decide how to effect it. Can be conscious = pathways which make it able for us to feel legs/arms etc, terminate on cortex. Or unconscious = those pathways are terminated in cerebellum for balance, position.
Static proprioception = to feel body position.
Dynamic proprioception = kinesthesia = to feel body and limb movements.

Reflex arch



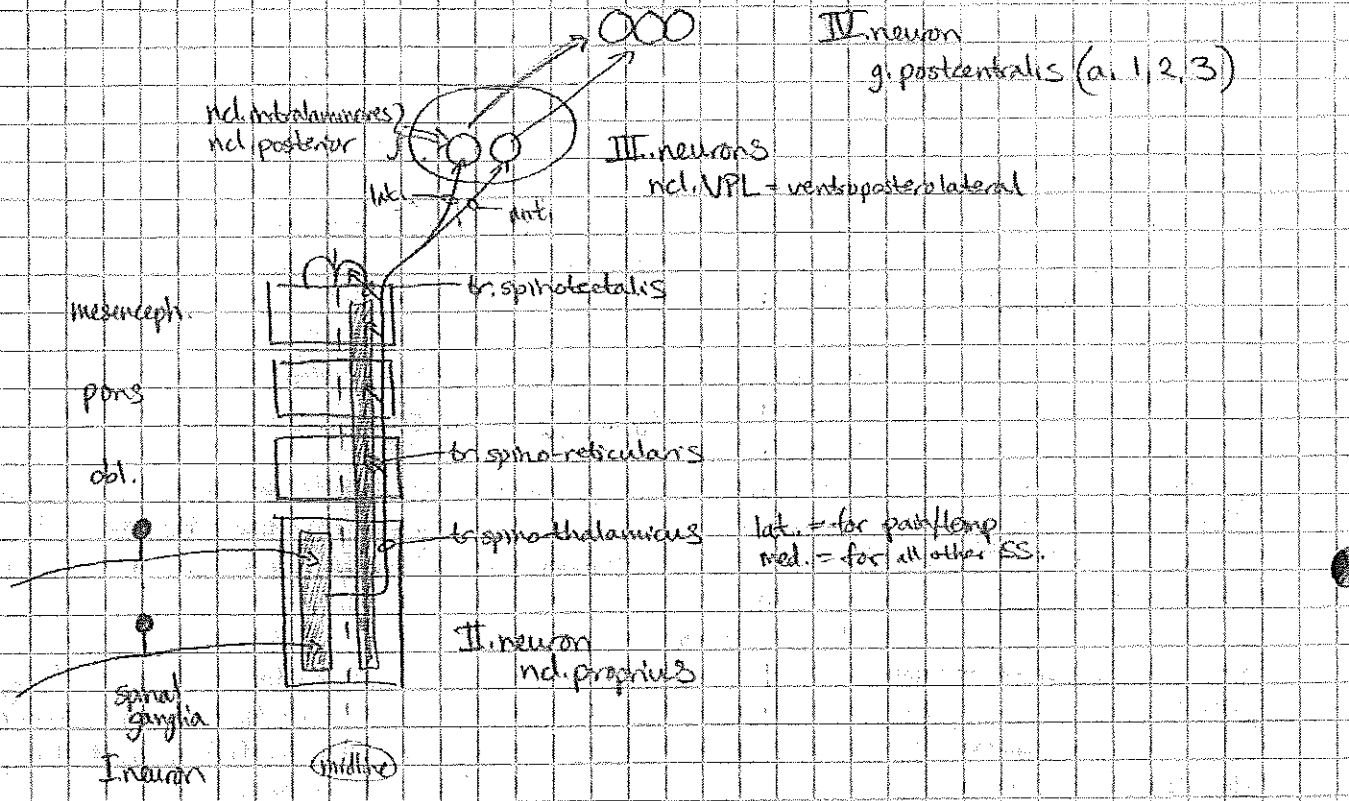
Stimuli from environment are caught + transformed into nerve impulses in sensor. Impulls is transmitted by sensory nerves to CNS. The central branch of pseudounipoll reach in spinal ggl. terminate on an interneuron which send info to motor neuron in CNS. This motor neuron respond by sending axons to effector.

Control + regulation of the effector response is recieved by proprioreceptors, they send info back to CNS via sensory nerves.

Somatosensory system is divided into: { lemniscal system, anterolateral system, trigeminal system } →

Anterolateral system, description, modalities & functions

Modalities: light skin touch, heat, cold, nociception



IIst order neurons = pseudounipol. in dorsal root ganglia. Their central branches enter spinal cord, terminate on IIrd neurons in ncl. proprius. Their axons cross midline and climb up to constitute the white matter column termed as tr. spino-thalamicus. It goes through brainstem to thalamus to IIIrd in ncl. ventro-poster-lateralis. It's a relay station for projection of signals to cortex for touch, heat/cold, pain.
Some axons will terminate on ncl. intralam. + post. (for pain).

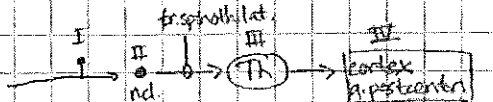
Besides termination in thalamus, some fibers terminate in other structures like reticular formation ⇒ constitute tr. spinoreticl. or they can terminate on tectum in mesencephalon ⇒ tr. spinotectalis. These pathways are also imp. for pain.

Ascendent pathways for pain:

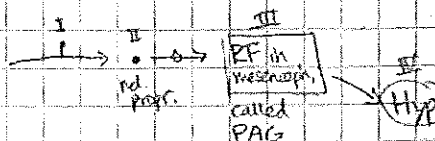
tr. spinothalamicus lat. – sharp, localized pain.

tr. spino-reticulo-thalamicus – diffuse, dull pain.

tr. spino-tectalis ⇒ emotional expression of pain.

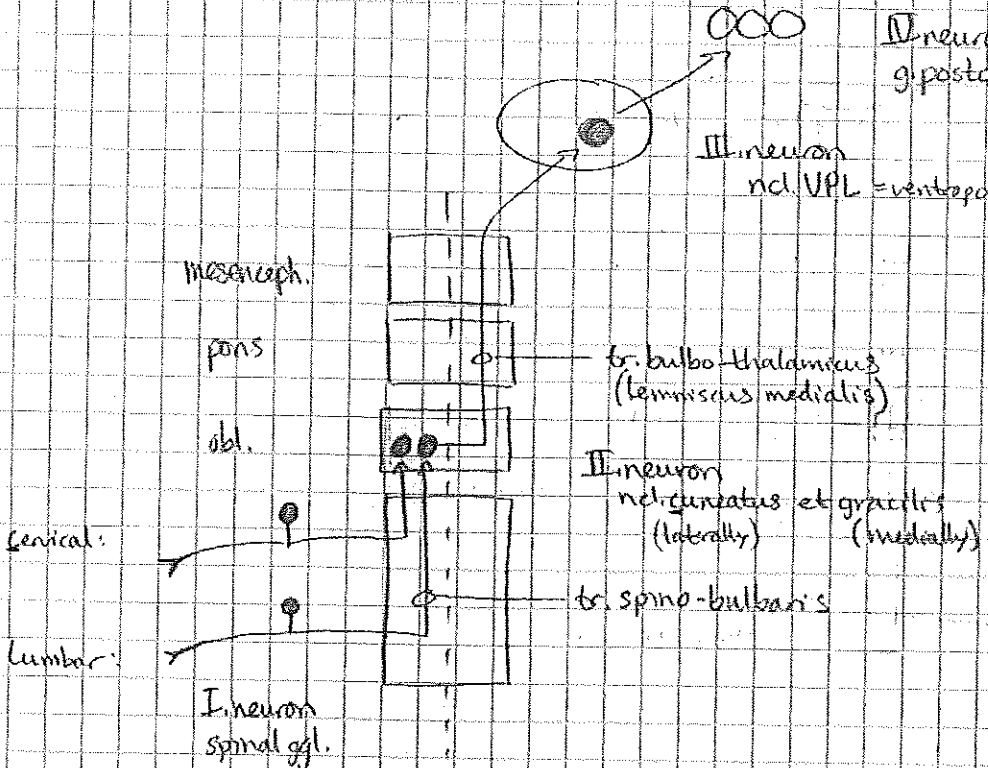


the will stimulate ♡ beat ⇒ will make your face turn red !



Lemniscal system, description, modalities, function

Modalities: tactile sensation (touch), vibration, stereognosia, conscious static + dynamic proprioception

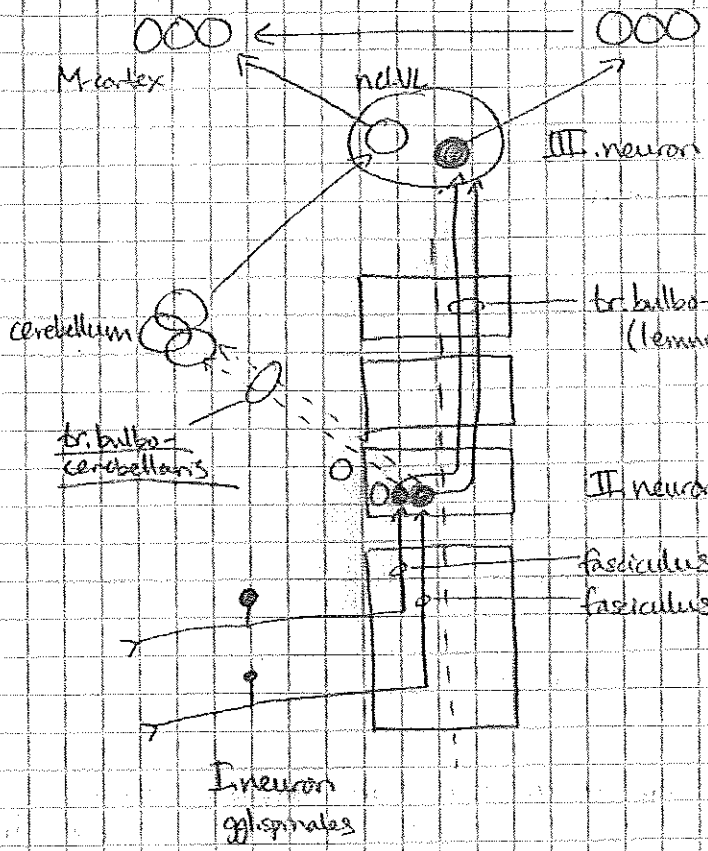


I are localized in lumbar + cervical position. Axons pass through spinal cord in fasciculus gracilis et cuneatus as tr. spino-bulbaris.
Cuneatus receives signals from cervical + upper thoracal o gracilis from lumbar + sacral segments. This is the somatotopic arrangement of these compartments.

The central branches of I don't cross midline. They keep the same side = ipsilateral side. II send axons which cross midline in level of obl. and terminate on III. Path is called tr. bulbo-thalamicus which goes in a column called lemniscus lateralis.

Imp. to know where crossing of midline occurs, because unilateral damage of spinal cord cause damage in contralateral cord.

Pathway for static proprioception = to feel body position. Conscious = makes us able to feel. Unconscious = for our balance

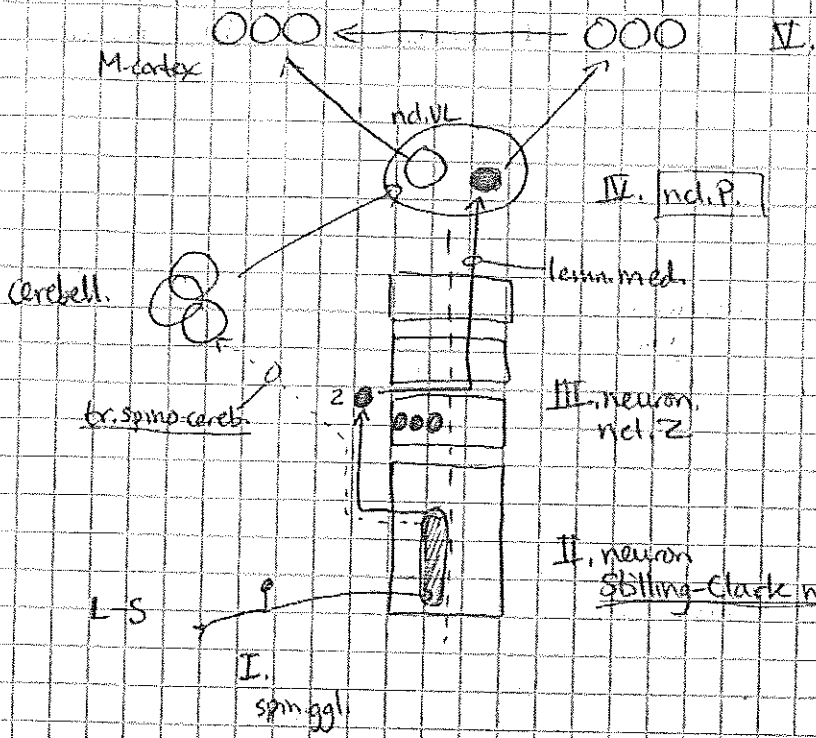


This pathway send signals to our chef structures which drive our conscious/unconscious movements.
II in upper + lower segments of spinal cord travel to ncl. gracilis + cuneatus.
II send axons in medial lemniscus, but they terminate on ncl. posterius in thalamus.
⇒ this is the pathway for conscious static proprioception.

For unconscious static proprioception axons from II can also be sent to cerebellum by the way of tr. bulbocerebellaris in pedunculus cerebel. inf.
Cerebellum elaborate these signals and convey them to thalamus, to ncl. ventro-lateralis.
These neurons convey signals to motor cortex-neurons located on gyrus precentralis.
They send signals to our unconscious movements.
There is also a communication btw M-cortex and g. postcentralis.

← ⊕ Proprioceptive pathways from upper/lower extremities

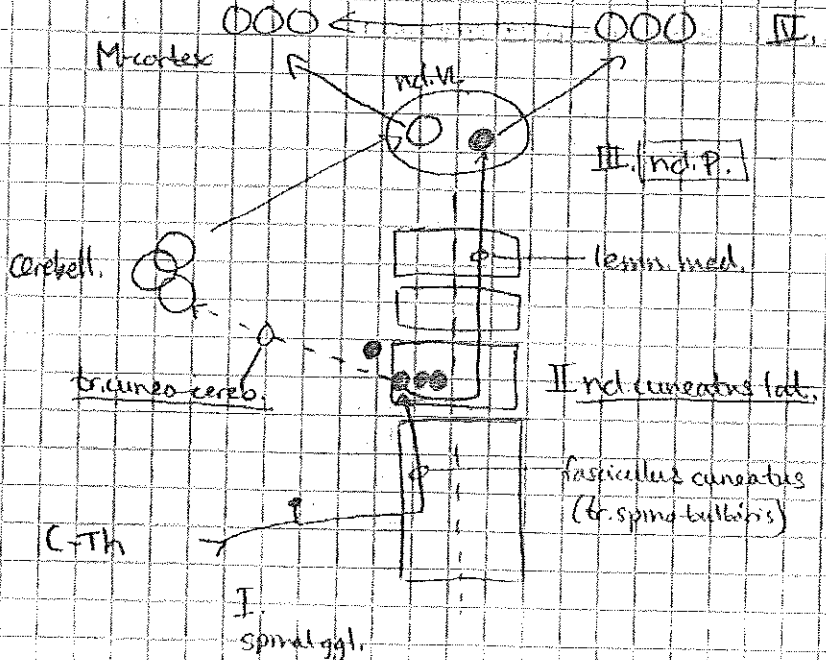
Pathway for dynamic proprioception - kinesthetic propr. (from L-S spinal cord)
⟹ to feel body & limb movem



IV. g. postcentr.

From L+S segments I terminate their central branches on Clarks ncl. at L1-Th1. II axons go to dbl. to a nucleus called ncl. Z. This nucleus is present on same side as axons (=ipsilateral). III axons climb up in lemn. med to thalamus. IV send signals to cortex. Signals recieved are about conscious propr. for our legs. It makes us able to feel th movements of our legs. It is used together with our motor activity.
Clark also send axons to cerebellum in tr. spino-cereb. Again signals via ncl. VL to M-cortex ⟹ unconscious propr for our legs

Pathway for kinesthetic propr. (from C-Th spinal cord segments)



IV. g. postcentr.

From C-Th segments I terminate on ncl. cuneatus lateralis. I travel in tr. spinobulbaris. II go in lemn. med. → thalamus → cortex ⟹ for conscious kinetic propr. of our hands = for movements of our hands without other sensation.

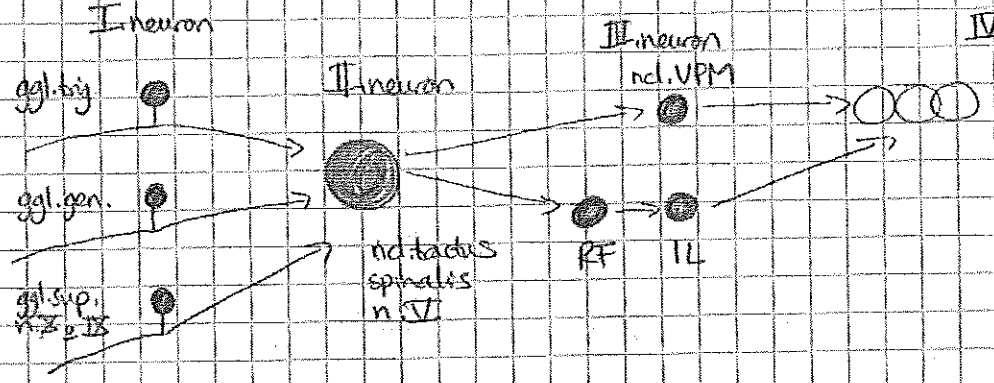
II also send axons in tr. cuneocerebell. ⟹ for unconscious kinetic propr. of our hands.

Trigeminal system

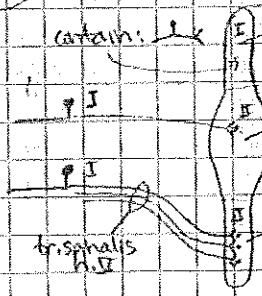
Distribution of the first and second order neurons in trig. system, description of modalities

All modalities from face part of head. Skin + mucous + muscles.
Proprioception from all these parts is analyzed by cortex by the way of trig. pathway.

Trigeminal pathway for light touch (protective)



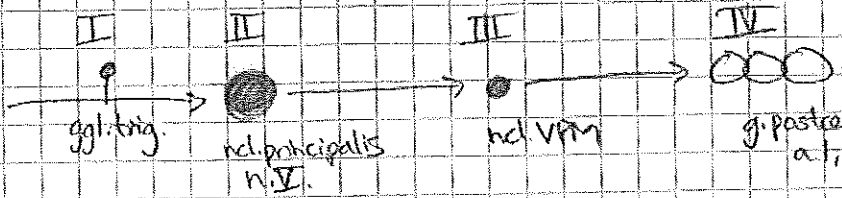
I neurons are present in ggl trigeminale, but also in ggl. geniculi (this ggl. also contains taste for taste pathway, see taste pathway) and ggl. sup. n. IX et X.
Central branches of these neurons enter brainstem and terminate on II neurons which form a column called ncl. tr. spin. n. V.



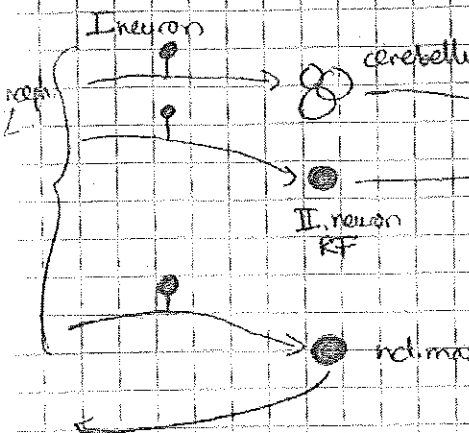
II send axons to thalamic nucleus, ncl. ventro-postero-med. III. to cortex. Cortex analyze our feeling of light touch, temp. etc. from our lips, mucous membranes etc.

There is also an additional pathway through reticular formation to intralaminar nucleus in thalamus to cortex
⇒ pathway mainly for pain.

Trigeminal pathway for discriminative sensation (tactile sens.)



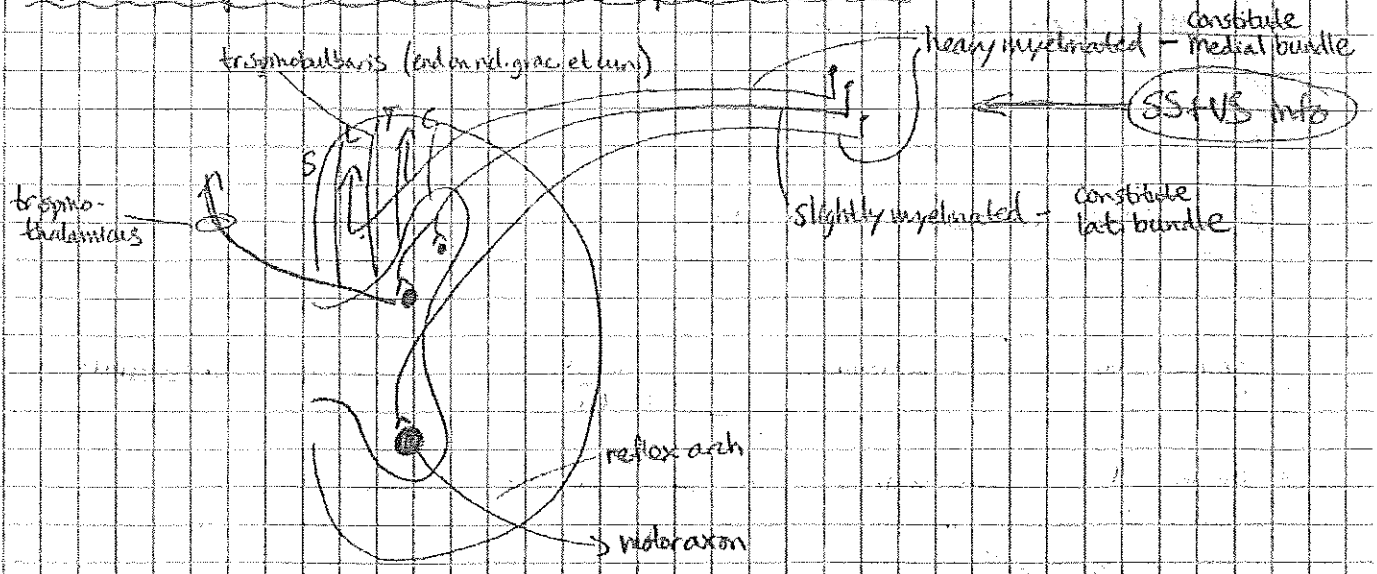
Trigeminal pathway for proprioception



I in ncl. mesencephalicus n. V send unconscious tension through cerebellum to cortex.
Or conscious sens. through reticular formation and thalamus to cortex.

Some other I neurons send axons to masticatory nucleus which then send motor to masticatory muscles.
= chew reflex arch. = protect teeth during chewing. Sensory neurons sense the press. of muscles → send to ncl. mest. → send info how much they can contract.

Entrance of somatosensory fibers to spinal cord, their description and connection to spinal neurons



Description see next page ! →

Medial bundle = all sensations except pain/temp.
Axons from lower part of body = more medially (gracilis) } ⇒ se lemniscal system
– " – upper – " – = laterally (cuneatus) }

Lateral bundle = pain/temp. + "light touch"
Axons travel in tr. spinothalamicus.
Tr. spinothal. lat. = pain/temp. } ⇒ se anterolat. system
– " – ant. = "light touch" }

Somatotopic arrangement of cortex

= on cortex we can reflect the parts of the human body, called homunculus.
Homunculus is a distorted human figure drawn to reflect the relative space human body parts occupy on the somatosensory cortex (sensory homunculus) & on the motor cortex (motor homunculus).
Ex. in motor homunculus large area is occupied by hands + mimic muscles + tongue.
In sensory homunculus – " – – " – hands + face.

→

Somatotopic arrangement of the somatosensory pathways and cortex

Somatotopic arrangement means that particular areas of the body are being centered in a specific region of the cortex.

Ist order neurons in spinal ggl. convey signals from somatic and visceral sensory receptors. Their central branches enter dorsal root and synapse on IInd order neurons in post. horn. in spinal cord.
The Ist order neurons are divided into 2 classes:
- Large neurons with heavy myelinated axons
- Small neurons with light myelinated axons

These 2 diff axons will become segregated inside spinal cord as a <u>medial bundle</u> with thick axons and a <u>lateral bundle</u> with thin axons.

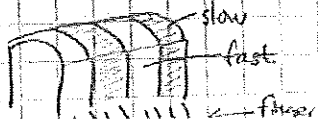
- The medial bundle convey impulses for sensation other than pain and temp.
  Most of the axons in this bundle ascend without synapses as far as to medobl. to form <u>tr. spino-bulbaris</u>
  Some of the axons will however terminate on motor neurons, constituting the <u>reflex arch</u>
  <u>The somatotopic arrangement of medial bundle:</u> terminate on gracilis
  Axons from lower part of body (sacral + lumbar segments) are located more medially
  and axons from upper part of body (thoracic + cervical segments) are located more laterally, terminate on cuneatus
- The lateral bundle convey impulses about thermal + pain sensation. The axons from I neurons enter grey matter of dorsal horn, and then travel in <u>tr. spinothalamicus</u> up.
  This tract has also <u>somatotopic arrangement.</u>
  First of all it is divided into a <u>lateral spinothalamic tract</u> and an <u>anterior spinothalamic tr.</u>
  Ant. → convey impulses about pain & temp. } ⇒ <u>ex anterolat system!</u>
  Lat → impulses about "light touch"
  The lat. one is further somatotopically arranged depending on which segment the axons came from (S, L, T, C).

<u>Syringomyelia</u> = is a disorder when a cyst or cavity forms within the spinal cord, it is filled with CSF. It can expand or elongate with time. This will damage the cord and loss of function in corresponding structures, the ability to feel extreme hot or cold in hands for example.

<u>There are also other somatotopically arranged areas in the somatosensory pathway:</u>
<u>In thalamus</u> – the VPM - ventroposteromedial nucleus recieves axons from face + tongue
the VPL - ventroposterolat. nucleus recieves from rest of body.

<u>In trigeminal system</u> – the II neurons in nd. spinalis n. V are arranged according areas of face:

The cortex is also somatotopically arranged. Higher sense regions of our body occupy larger fields on cortex, ex. hand, face, tongue, fingers. We can construct <u>homunculus</u>.
Ex. In gyrus postcentralis, also somatotop. arrang. as area 3, 1, 2.
Area 3 = muscle proprioception + slow addaptation receptors from skin
Area 1 = fast addaptation receptors from skin.
Area 2 = proprioception from joints (pressure and position)
In this gyrus we can distinguish some columns through all layers of cortex which elaborate signals from fast or slow addaption receptors from fingers.



Pathways of the visceral sensation

viscera, glomus aort., sinus caroticus → ggl. inf. n. IX, ggl. inf. n. X → I neurons → nucl. solitarius → Thalamus → VS cortex

Axons of viscero sensensation are present ("hitch a ride") inside nerves of para. symp.
The Ist order neuron of visceral sensation is located in ggl. inf. n. IX. They are pseudounipolar. Their peripheral branch terminate on sensors located in wall of viscera ex: in oesophagus, ...
Some Ist order neurons have their peripheral branch on baroreceptors in sinus caroticus and some other Ist have periph. branch on chemoreceptors in glomus caroticus.
All central branches from Ist terminate in nucl. solitarius.

Nucl. solitarius is the main nucleus for viscerosensation. It contains IInd neurons of this pathway, but also neurons for taste pathway.

IInd order neurons:
→ taste pathway
→ respiratory nucleus = here terminate Ist from glomus caot. / monitor level of O_2 & CO_2
→ baroreceptor nucleus = " " " sinus caot. / monitor BP
nucl. commissuralis here terminate Ist from viscera.

Some other Ist order neurons are present in ggl. inf. n. X. Their peripheral branches terminate on walls of viscera ex: heart, respiratory system + alimentary tract.
Other peripheral branches terminate on sinus caroticus & glomus caroticum.
Their central branches also terminate on nucl. solitarius.

In nucl. commissuralis terminate the central branches which convey info from viscera.
Nucl. solitarius send further info to cortex.

Visceral sensation – stimuli, receptors, their distribution

Is a part of ANS, most visceral receptors are supplied by free nerve endings.
Receptors are similar to them in skin, but in viscera there are less temp. & touch receptors, and there exist no proprioreceptors in viscera.
Pain receptors are distributed in periosteum, arterial wall, joint surfaces and walls of viscera.

Baroreceptors = sinus caroticus = detect pressure of blood & ↑ or ↓ cardiac output.
Chemoreceptors = glomus caroticus = detect changes in blood O_2, CO_2 & pH (H^+ level).
Osmoreceptors = in hypothalamus = control fluid balance in body.

Baroreceptors are a type of mechanoreceptors, when stretched send signal to nucl. solitarius which sends further signals to ↑ or ↓ cardiac output.

Chemoreceptors: central ones (medulla obl.) = detect changes in H^+ level in CSF
peripheral ones (glomus caroticus, glomus aorticus)

Referred pain

Viscerosensation neurons and pain sensation mix.
Cortex recieves a mixture of signals and misinterpret.
The feeling of pain is in an other location than the source. Ex during ♡ attack.

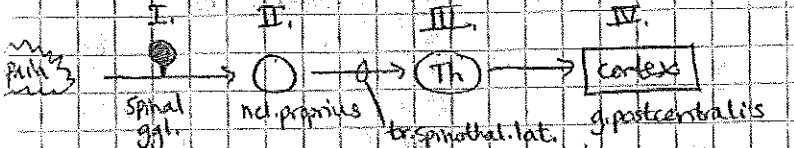
Ascendent pathways for the nociceptive information; schema & description

Pain is a warning signal to organism. Nocisenzors - activated by mechanic, thermal, chemical stimuli; factors which damage tissue.
Noxios stimuli is conveyed in 2 axons:
- Aδ = are myelinated ⇒ high speed 5-30 m/s. Sharp, localized pain.
- C-fibers = unmyelinated ⇒ slow, 0,5-2 m/s. Pain is dull, can't really localize the origin of it.

Pathways

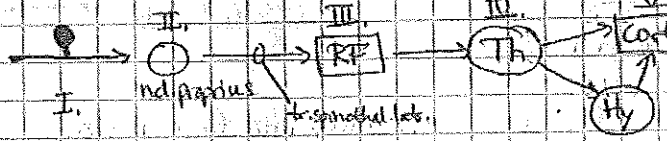
Lateral pain system = consist of tr. spinothalamicus lat. It's associated with sharp, localized pain.
Medial pain system = consists of spinoreticulothalamic and trigemino-reticulo-thalamic pathways. Involved in diffuse, dull pain. This system is connected with limbic syst. & therefore it drives our behavior to pain (use bad words, cry etc...).

Tr. spinothalamicus lat. - sharp, localized pain.



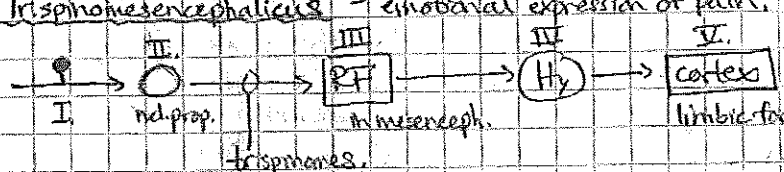
After nd. proprius axons cross midline & enter tr. spinothalamicus (divided into ant. & lat. The lat. is for pain)

Tr. spino-reticulo-thalamicus - diffuse, dull pain.



A part of axons in tr. spinothal. lat. will terminate on RF (= tr. spino-reticul.) → then go to thalamus (tr. reticulothal.) Signals will go to frontal & limbic ⇒ drives our behavior to pain.
Hypothalamus will stimulate ♡ beat & you'll change color of face to red.

Tr. spinomesencephalicus (spinotectalis) - emotional expression of pain.

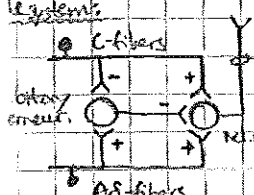


This pathway go via hypothalamus (not thalamus) and into RF around Sylvian channel called periaqueductal grey & to RF.

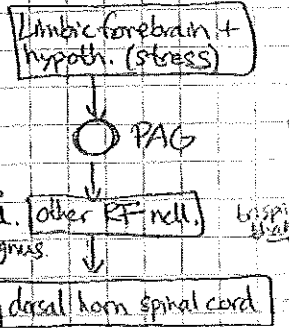
Trigemino-reticulo-thalamic pathways - tr. trigemino-reticulo-thalamicus = diffuse pain
tr. trigemino-thalamicus-ventralis = sharp pain.

Nociceptive analgetic system

Nociceptive info which reach body is modulated in many levels:
Spinal level - according to gate system. I neuron terminate on nd. propr. Stimulate it to send info to upper structures. In dorsal horn we have some interneurons which can inhibit activity of neurons in nd. proprius. They make signal to ↓ in tr. spinothal. However, some fibers from I neuron can stimulate or inhibit the interneurons: C-fibers - inhibit. interneurons ⇒ nd. prop. activity ↑ ⇒ gate is open!
Aδ - activate interneur. ⇒ nd. prop. activity ↓ ⇒ gate is closed!



Supraspinal level:
Structures are involved in reducing pain sensation.
= stress induced analgesia.
Limb + hyp. send signals during stress to PAG.
They influence other RF nuclei which influence dorsal horn. Neurons in dorsal horn send axons in tr. spinothal ⇒ reduce pain to upper structures! RF use serotonine which stimulate



Enkephalin bind to opioid receptors and act as natural pain killers!

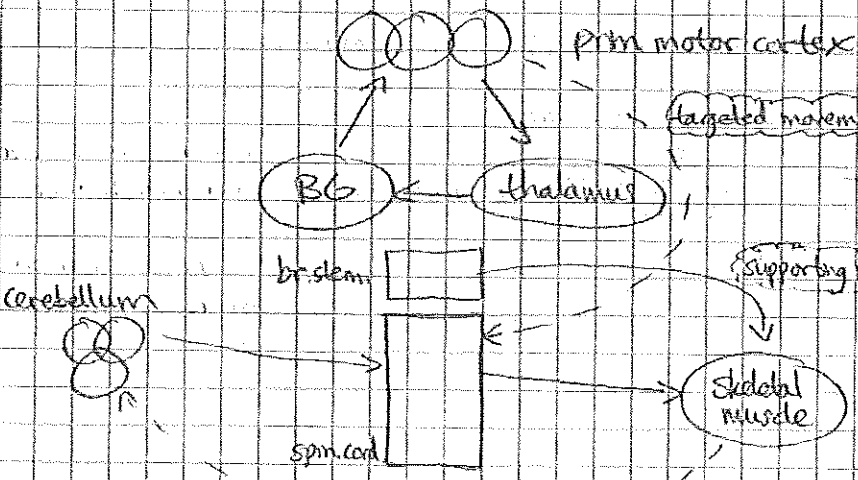
Hierarchic organization of motor system, classes of movements

Motor system = structures which drive our movements.
We have motor neurons at different levels:

In spinal cord, M-neurons innervate skeletal muscles. Proprioasensors in muscle spindles & somatosensory sensors in skin send info back through spinal cord and reach cerebellum. It will elaborate signals back to motor neurons & influence/modulate their activity.

At level of brainstem we also have structures which drives our movements. These signals sent to the muscles are imp. for keeping the tone of the muscles, eg. when we're in upright position. ⇒ so called supporting movements.

Then we have other subcortical structures which also drive our movements, eg. BG & thalamus. They are connected with primary motor cortex.
The cortical & subcortical structures are responsible for our conscious movements. They form a circle and send signals to so called targeted movements.
The last signal from prim. motor cortex is sent to spinal cord.



Main structures in motor system:
- Cortex
- Brainstem
- Spinal cord

Other mo structures
- Cerebellum
- BG
- Motor thalamus (nct. ventralis ant. et lat.)

Classification of motor movements

Targeted movements: • voluntary movements, eg. when want to move a hand, grab something.
• also motor control of tongue, lips, breathing etc. so we can control our speech.

- Supporting movements: • to maintain posture & position of body.

Emotional motor movements: • motor expression of our feelings. Serves for our communication. Ex. to express our mimik muscles to make face expression.

- Voluntary movement = targeted and purposal movement. Stimulated by our will.
- Reflex movement = simple movement reaction to external stimuli. A stereotypical fast movement (supporting movement). Is at minimal influence of will. But we can depress the reflex and keep our fingers on the hot plate even if it hurts.
- Rhythmic motor movement = the beginning & finishing of the movement is voluntary, but inbetween it's stereotypical. Ex. walking. We decide when to start/stop. But we don't think how we walk inbetween it's

Sensory information necessary for the control of movements

Structures supplying control of movements:
- Spinal cord
- Brainstem (NR, SN, RF, olivary nucleus, vestibular nucleus)
- Cortex
- Cerebellum
- BG
- Motor thalamus (ncll. ventralis et lateralis)

Lower motorneurons - brainstem:
- Somatomotor zone: ncl.o.n. III, IV, VI, XII
- Brachiomotor zone: ncl.a n. V, VII, IX, X

(brainstem + cortex)

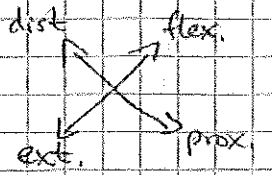
Motor systems for control of movements: – Upper motor structures send info to spinal cord motor neurons via 3 systems.
- Medial system
- Lateral system
- 3rd motor system

To control our movements we need proprioception and afferentation from somatosensory system.

Motor system

Motor neurons in spinal cord are organized in columns in ventral horn.
One column is called medial column and it's located medially. It participate in innervation of striated muscles close to our midline.
The other column is called lateral column and is located laterally. It innervates muscles located more laterally in our body.

In lat. column:
- flexors are located more deep
- extensors – " – superficial
- distal muscle groups = extremities (ex. arms) are located more laterally.
- proximal muscle groups of our extremities (ex. shoulders) are located more medially in column.



In brainstem we have two types of motor neurons:
- In somatomotor zone – ncll. origins nn. III, IV, VII, XII ⇒ for motor driving of our eyes and tongue
- In branchiomotor zone – ncll. origins nn. V, VII, IX, X ⇒ for motor driving of our mimic muscles, larynx/pharynx & masticatory mm.

These neurons send info to motor neurons in spinal cord in 3 systems:
- Medial system
- Lateral system
- Third motor system – driving of our emotional movements.

Medial system can be divided into 2 pathways:
- Brainstem pathway
- Cortical pathway

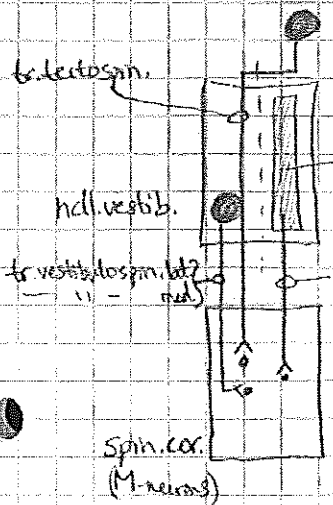
Lateral system can also be divided into 2 pathways:
- Brainstem pathway
- Cortical pathway

(System of med pathways from brainstem that influence spinal cord M-neurons, their function)

Medial system – {Brainstem pathways}

ncl. coll. sup. in tectum are connected with spinal cord with tr. tectospinalis. It crosses midline.
Ncll. vestibulares & RF are also connected with spin. cord.

> Med. system = for postural movements, to keep posture + coordination of head & eye movements.



tr. tectospinalis terminate on spinal segments on neck.
Of course cortex will control this tract by forming tr. cortico-tectospinalis.
tr. reticulospinalis can be divided into medial + lateral tr.
Lat. → from RF in obl. will project on neurons in spin. cord which activate/inhibit extensors.
Med. → from RF in pons – will activate extensors & keep their tonus.
Of course there is a tr. cortico-reticulospinalis as well here!

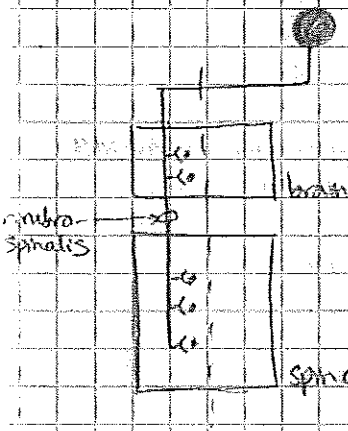
tr. vestibulospinales terminate on α-motorneurons & γ-motorneurons. They have direct control over α-neurons.

ncl. vestibularis lat. (Dieters) – send tr. vestibulospin. lat. Go on same side (ipsilaterally) to lower motor neurons. It innervates all moter neurons in spin. cord. It controls extensors.

ncl. vestibularis med. (Schwalbe) – tr. vestibulospin. med. Innervate only neck motor neurons. It descends bilaterally and end on C-Th segments. It controls neck muscles.

Cerebellar cortex send axons to ncll. vestibulares and inhibit them.
If non function of cerebellum → uncontrolled excitation of α-motorneurons.

Lateral system – brainstem pathways ← System of lat. pathways that influence spinal M-neurons, their function.



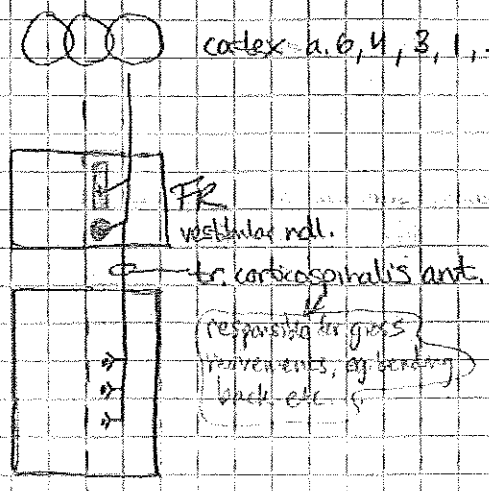
In lat. system the main structure is ncl. ruber. Axons cross midline and constitute tr. rubrospinalis.

(ncl. ruber is located in tegmentum. It's composed of 2 regions: caudal region is magnocellular & rostal is parvocellular.)

tr. rubrospinalis descends in the lateral part of brainstem tegmentum and in the spinal cord it travels through funiculus lat. in the company of tr. corticospinalis lat.

This tract is the main route for mediation of voluntary movement. It's responsible for large muscle movements such as arms and legs as well as fine motor control. It facilitates flexion and inhibit extension in the upper extremities.

Medial system – cortical pathways ← System of med. cortical pathways that influence spinal motorneurons, their function



Medial system participate in voluntary innervation of neck, body and proximal muscles of extremities.

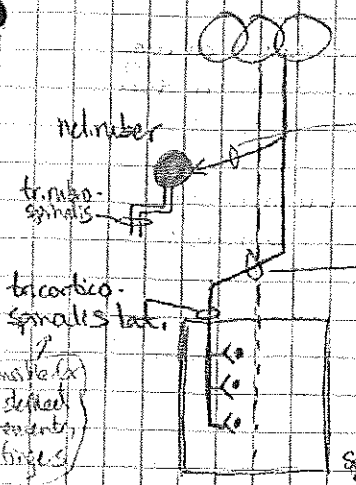
Axons start in primary motor cortex in gyrus precentralis, in areas 3, 1, 2 and in a. 6 and 4.

Axons run bilaterally to medial group of lower motorneurons.
Some axons terminate on neurons of medial motor system of brainstem constitute tr. cortico-vestibulo-spinalis & tr. cortico-reticulo-spinalis.

Med. system don't cross midline!
(Lat. do!)

Lateral system – {cortical pathways}

{System of the cortical pathways that influence spinal M-neurons, their function}



Lateral system also begin in cortex.
Axons will cross midline and constitute decussatio pyramidum on brainstem.
Then travel to spinal cord in tr. cortico-spinalis lat.

> tr. corticospinalis lat. innervate distal muscles of extremities and the movements are voluntary.

Some axons will also terminate on nel. ruber, constitute tr. cortico-rubro-spinalis.

In both lateral and medial cortical pathway systems
ca 30% of axons come from a. 4 in gyrus precentralis.
ca 30% from a. 6 in frontal lobe (infront of g. precentr.)
ca 40% from a. 3, 1, 2 in lobus parietalis. A part of these axons terminate on gracilis and cuneatus nuclei for modulation of the afferent signals!

Motor cortex ← {Role of cortical motor areas in motor control}

Primary motor cortex = a. 4 (g. precentr.)
- somatotopic arrangement
- direct exitatory influence of motoneurons of motor units.

Motor unit = the connection btw one motoneuron axon with a nr. of muscle fibers.
Small motor unit: 1 motoneuron innervates a few muscle fibers. Where we need very fine motor movements. Ex. oculomotor muscles, hand muscles.
Large motor units: 1 motorneuron innervates 500-1000 muscle fibers, ex. back muscles. Here the movements are not so fine.

Secondary motor cortex:
Is subdivided into:

PMC
- Premotor cortex = a. 6 at the lateral surface of frontal lobe.
  - control medial brainstem system
  - control proximal muscles of extremities

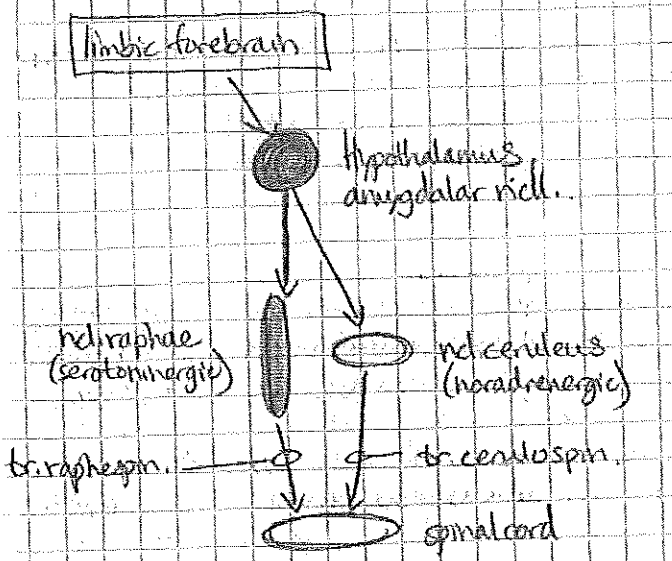
SMA
- Supplementary motor area = a. 6 at the medial surface of frontal lobe
  - stimulate complex movements like opening or clasp of fist.
  - imp. for the planning of contraction/relaxation of muscles. We plan our coordinated movements here!

PMA
- Premotor area = parietal cortex, a. 5, 7
  - for integration of SS & S info. Imp. for planning of voluntary (targeted) movements

- Frontal eye field = anterior cingular convolution, a. 23, 24.
  - specialized for the driving of our eyemovements = voluntary movements, during following an object.

PMC + SMA don't contain motor neurons, but are imp. for preparation of M. cortex to send signals to lower spinal cord motor neurons.

The third motor system



LF is connected with hyp. + amyg. and these structures are connected with brainstem nuclei called nd. ceul. + nd. raphe, which are connected to motorneurons in spinal cord by tr. raphespin. o tr. ceruleospin.

By this way we control our mimic movements during emotional activity.

Muscle spindles and Golgi tendon organs, structure and function

Skeletal muscles have 2 mechanosensitive proprioceptors: muscle spindles o Golgi tendon organs. A muscle contains two kinds of muscle fibers: extrafusal fibers that cause muscle contraction and intrafusal fibers which lie parallel with the extrafusal fibers. Some of the extrafusal fibers have Golgi tendon organs located between the end of the muscle fiber and the tendon. The intrafusal fibers contain muscle spindles, which receives both aff. (sensory) + eff. (motor) innervation. The spindle contains both bag fibers, with nuclei bunched together and chain fibers with nuclei in a row.

(proprioception)
Golgi tendon organ = consist of bare nerve endings encapsulated by a collagen matrix. They are located btw skeletal muscle fibers o the tendon. When tension develops in muscle due to contraction, the collagen fibers tend to squeeze and distort the nerve endings which trigger them to fire action potentials.
Their function is to measure the force generated by a muscle by measuring the tension in its tendon.

(alterations)
Muscle spindle = measure the length of the muscle and how much it is stretched.
Consist of two muscle fibers (bag and chain) with two types of sensory endings entwined around them (primary and secondary endings).
Primary sensory endings coil around bag muscle fibers, they are sensitive to changes in the length of muscle.
Secondary sensory endings innervate chain fibers, they convey info about the static length of the muscle, they are slowly addapting receptors.

- See better description Proprioception! → längre fram!

Alfa and gamma motoneurons, their function

There are 2 types of motoneurons:
α-motor neurons = innervate the force-generating muscle fibers (the extrafusal fibers which do the contraction). Are located in ventral horn of spinal cord.
γ-motor neurons = innervate only the fibers of the muscle spindles. Are located within the muscle spindle.
The group of all motor neurons innervating a single muscle is called a motor neuron pool.

Stretch reflex → {see also reflexes in motor control q.!}
Besides skeletal muscle contraction, the α-motoneurons also contribute to muscle tone, imp. for our posture. When a muscle is stretched, sensory neurons in muscle spindle send info about the degree of stretch to CNS. The CNS activates the α-neurons in spinal cord and they cause the extrafusal fibers to contract and thereby inhibit further stretching because the length of it decreases. This is called the stretch reflex. The contraction increases the muscle tension, but decreases the stretch. This is imp. because this reflex allows spindles to be taut and therefore even sensitive during contraction. Function of this reflex is to maintain a constant length.

(homonymic)

This reflex is strong in extensor muscles. Ex is the knee-jerk reflex, by tap the patellar tendon. The tap move the tendon which then pulls on and briefly stretches the quadriceps femoris muscle.

(afferentation by Ia fibers, their dendrites are attached to intrafusal fibers = annulospinal nerve endings.)

γ-motor neurons innervate intrafusal fibers. Allow variation of their length and stretch sensitivity.
γ are regulated by upper structures.

Gamma loop
Golgi tendon organ reflex
Stretch reflex

Adaptation of sensory information

When a maintained stimulus of constant strength is applied to a receptor, the frequency of the AP sent away in the sensory nerve is declined during time. This phenomenon is called adaptation.

There exist rapidly adapting receptors and slowly adapting receptors.

Light touch appears to have rapidly adapting receptors and spindle and nociceptors are slowly adapting receptors.

Light touch would be distracting if it were persistent and input from nociceptors would loose its value if it adapted and disappeared.

Ex. We feel the light touch of our clothes when we first put them on our body, but after a while we stop feeling the touch of the clothes.

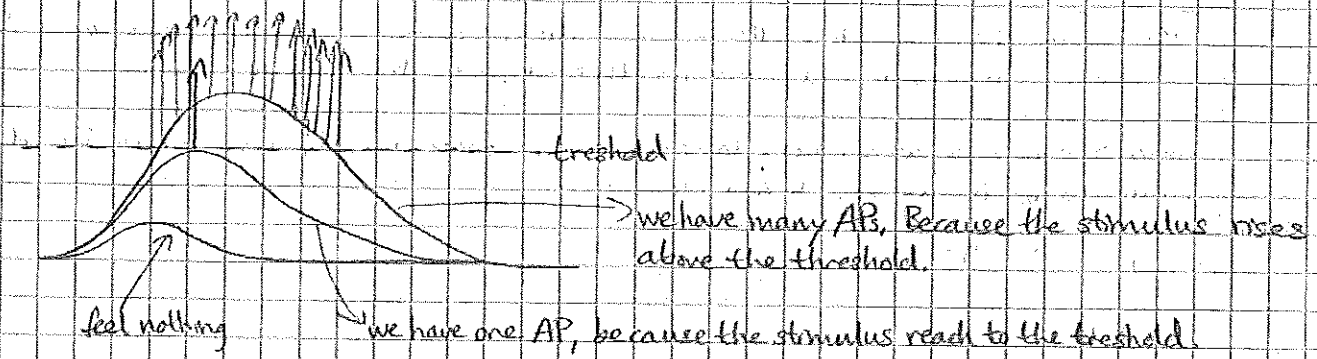
Same thing is if you smell something, but after a while you won't feel the smell because you've adapted to it.

Coding of sensory information

The speed of conduction in sensory nerve fibers vary, but AP are similar in all nerves. Ex. AP from touch receptor is the same as AP in a warmth receptor.
Why is stimulation from a touch receptor felt as touch and not as warm?
How is it possible to tell whether the touch is light or heavy?

- The sensation depends on which part of brain is activated.
- It also depends on the number of APs.

How do we know if a touch is gentle or hard?



We feel the difference because brain count the action potentials.
The magnitude of stimuli is transformed into number of AP.

Senses

Info from internal/external environment activate CNS via sensory receptors.
We have diff. sensory receptors: mechanical (touch-pressure), thermal (degree of warmth), electromagnetic (light), and chemical (odor, taste and O_2 content in blood).
These receptors are adapted to respond to one particular form of energy which is called adequate stimulus. Adequate stimulus for rods & cones = light.

Taste and smell

Taste and smell receptors are quite similar, because they both recognize molecules & convey info to CNS. However receptor cells of smell are neurons with axons, but taste receptors are not neurons, they are modified epi cells and axons of sensory neurons synapse on them.

Taste receptors are located on dorsal tongue inside papillae. Here they form taste buds, contains 50-150 receptor cells, + supporting cells, + sensory afferent axons. Most people have 2000-5000 taste buds. Apical end has microvilli that project into the taste pore. We can sense 5 primary taste qualities: bitter, salt, sweet, sour, umami (= "delicious" is the taste of glutamate). A single taste cell can respond to one, some or all basic taste groups. The tastants may pass directly into cell through ion channels or it may bind to and block ion channels or it may bind to membrane receptors that activate second-messenger systems which will open ion channels.

Ex. Salt = chemical is NaCl. When Na^+ rises outside the receptor cell, the gradient of Na^+ across membrane becomes bigger, Na^+ will go from high to low conc. ⇒ it will diffuse through ion channels into cell! This cause the cell to depolarize and send AP.

Ex. Sweets = is sensed when molecules binds to specific receptor sites and activates a cascade of second-messengers. Activated receptor cell activates a G-protein that stimulates phospholipase C to produce the messenger inositol-3-phosphate (IP_3) which will trigger release of Ca^{2+} from internal stores. This trigger a cation channel to open and this will depolarize the cell and it will send AP.

Smell receptors are located in olfactory ep. together with supporting cells. Olfactory cells (like taste cells) continually die and regenerate in cycles of 4-8 weeks. They are one of few neurons which are replaced regularly throughout life.
Before the odorants can contact the olfactory cells they have to pass through a thin mucous layer. The mucous consist of glycosaminoglycans, proteins like antibodies, odorant binding proteins & enzymes, and salts. The antibodies are imp. for fighting against viruses or bacteria to enter brain. The odorant-binding proteins help the odorants to diffuse towards the receptors.

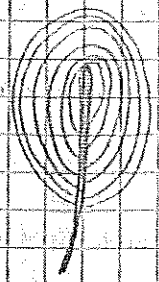
Surface area of human olf. ep ≈ 10 cm^2. Dogs have 170 cm^2 and more than 100× more receptors. Therefore dogs can detect the scent of someone who walked by hours ago.
We can smell more than 400 000 different substances. 80% of them smell unpleasant, probably an imp. protective function to warn us away from harmful substances.
Olfactory receptors use a second-messenger mechanism:
Odorant bind to a specific olfactory receptor in the cell membrane of a cilium of an olf. receptor cell. Receptor activate a G-protein. A subunit of G-protein activate adenylyl cyclase which produce cAMP. cAMP binds to cAMP-gated cation channel. Opening of this channel makes Na^+, K^+ and Ca^{2+} go into cell. This lead to a membrane depolarization. The increase of Ca^{2+} inside cell makes a Ca^{2+}-activated Cl^- channel to open. Opening of this channel produce even more depolarization. If the receptor potential exceeds the threshold it triggers action potentials.

Each receptor cell have binding sites for only certain types of odorants, and ca 1000 different types of olfactory receptor cells are present.
The termination of olfactory response occurs when odorants diffuse away or if enzymes of mucous layer break them down or if cAMP activates other signaling pathways that end the transduction process.

Touch - stimuli, receptors & their distribution

We can detect the sense of touch or pressure by means of mechanoreceptors located in the skin. They respond when the skin is vibrated, pressed, plucked or stroked or when its hairs are bent or pulled.
We have many different mechanoreceptors:

- Pacini's corpuscle - located in subcutaneous tissue. Has a capsule with 20-70 onion-like layers of c.t. and a nerve terminal in the middle. When capsule is compressed, energy is transfered to the nerve terminal, its membrane is deformed and mechanosensitive channels opens! Current flowing through the channels generates a depolarization, that if large enough causes axon to fire an AP.
However, the layers of the capsule are slick and can glide past another. So, if stimulus is maintained for a long time the layers will transfer the stimulus energy away from the underlying nerve terminal so it no longer become deformed. In this way the Pacini's corpuscle is unresponsible for steady pressure. Ex from clothes. Is a rapidly adapting sensor.



Respond to pressure + vibration.

Other types of encapsulated mechanoreceptors in skin are:

- Meissner's corpuscle - located in hairless skin, ex. lips, palms/soles. Cylinder-shaped.
- Ruffini's corpuscle - like pacini's located both in hairy/hairless skin in the subcut.tis. They resemble small pacini's. They respond to "fluttering" vibrations at low frequency. Is a slowly adapting sensor.
- Merkel's disks - also slowly adapting. Consist of flattened ep. cells that synapse on a nerve terminal. Found in hairless skin.
- Krause's end bulbs - around lips and external genitalia. Rapid adapting.

Two things determine the sensitivity of spatial discrimination in an area of skin.
1) the size of the receptor field of the receptor
2) the density of the receptors.
Pacini's have broad receptive field, but Meissner's & Merkel's have small. Small receptor fields are imp. for high spatial discrimination, eg on fingertips we have many Meiss & Merkel.
In fingertips we also have higher density of receptors which make them more sensitive than the palm.

Temperature sense — stimuli, receptors and their characteristics

Thermoreceptors are located in skin and they are divided into cold receptors and warmth receptors.
Like mechanoreceptors, the thermoreceptors are not distributed evenly across the skin.
You can map the skin with a warm or cold probe and find areas which are especially sensitive to either cold or hot, not both.
The cutaneous thermoreceptors are probably free nerve endings.

Warmth receptors: begin firing above 30°C and increase their firing rate until 45°C. Above this, the firing decreases steeply and a sensation of pain begins, mediated by nociceptive receptors.

Cold receptors: are quiet at 40°C, but as temperature falls they increase their firing rate until 28°C, then they decrease their firing rate until 10°C. Below that temp. they stop firing and you loose the sense in that area.

(Cold receptors are also able to report changes in temp.
Ex. when temp. shifts from 20,5°C to 15,2°C, the firing rate increases)

The transduction of warm temperatures are done with TRPV channels. These channels are sensitive to elevated temperatures. They are also sensitive to capsaicin, which is a component in spicy food. So hot chili peppers appears "hot" because it activate the same ion channel that is activated by heat.

The transduction of cold is done by TRPM8 channels which begin to open below temp 27°C. They are also sensitive to menthol, so menthol evokes the sensation of cold because it activates the same ion channel as cold temp.

Nociception, pain — stimuli, receptors, physiological significance.

Nociceptors are the receptors mediating painful feelings to warn us that body tissue is being damaged or is at risk of being damaged.
Nociceptors can be:

- Mechanical nociceptors = which respond to strong pressure, especially by sharp objects.
- Thermal nociceptors = signal either burning heat (above 45°C) or unhealthy cold.
- Chemically sensitive nociceptors = respond to diff. agents such as K^+, extreme pH, histamine from body itself or various irritants from environment.
- Polymodal nociceptors = are single nerve endings that are sensitive to combinations of mechanical, thermal and chemical stimuli.

Nociceptive axons include both fast myelinated Aδ-fibers and slow unmyelinated C-fibers.
Aδ-fibers mediate sensation of sharp, intense pain.
C-fibers mediate sensation of dull, burning pain.

Nociceptors are free nerve endings, widely distributed throughout body. They innervate skin, bone, muscles, internal organs, vessels & heart. However they're absent in brain, but exist in meninges.

Sense of balance - stimuli, receptor cells

The vestibular system generates our sense of balance. Vestibular sensation operates constantly while we are awake and gives info to brain about the head's orientation and the changes of head's motion.

Otholit organs in saccule and utricle detect the linear acceleration of head.

Crista ampullaris in semicircular canals detect the angular acceleration of head.

The otholit organs as well as semicircular canals are lined with ep. cells and filled with endolymph. Within the ep. a specialized vestibular dark cell secretes K^+ and are responsible for the high K^+ conc. of endolymph.

Each saccule & utricule has a sensory ep. called macula. Macula contains the hair cells together with supporting cells. The stereocilia project into gelatinous layer which contain otoliths. When move our head the otholits follow and deflects the stereocilli.
Macula is vertical oriented in saccule and horizontally in utricule.

Each hair cell synapses on the ending of a primary sensory axon, which is a part of vestibular nerve.

In semicircular canals their hair cells are located within a sensory ep. called crista ampullaris
They project into a gelatinous structure called cupula.
When the canal suddenly rotates due to movement of the head the endolymph inside canals tends to stay behind because of inertia. This makes cupula to bend, which bends the hair cells and they fire an AP to vestibulur nerve.

Each side of head has 3 semicircular canals. Ant., post. & lat.

Proprioception - stimuli, receptors, their distribution

Proprioception provides sensation about the body itself to know where each of its parts is in space.
Skeletal muscles which mediate our voluntary movement have 2 mechanosensitive proprioceptors: the muscle spindles and Golgi tendon organs.

Golgi-tendon organs - located within the extrafusal muscle fibers. Consists of bare nerve endings of group Ib axons. At junction of tendon/muscle.
They are encapsulated with collagen fibers, so when muscle tension develop, the collagen fibers squeeze and distort the nerveendings making them bigger AP.

Muscle spindle - located in intrafusal muscle fibers.

In addition to muscle receptors, various mechanoreceptors are found in the c.t. of joints, esp. within capsules & ligg. Many of them resembles Ruffini, Golgi & Pacini, others are free nerve endings. They respond to changes in the angle, direction, and velocity of movement of joint.

Measure the length of the muscle and how much it's stretched.
Innervated by Ia fibers. Their dendrites are attached to intrafusal fibers
→ Afferentation will go in Ia fibers to spinal cord where they stimulate α-motorneurons to contract antagonist → thereby ↓ stretch.

(- See also Reflexes in motor control!) → bigger form!

Visceral sensation - stimuli, receptors, their distribution.

Is a part of ANS. Most visceral receptors are supplied by myelinated & unmyelinated fibers that terminate as free nerve endings.

Receptors are:

Osmoreceptors - found in hypoth. Control fluid balance in body.
Baroreceptors - detect pressure of blood and can ↑ or ↓ cardiac output.
Chemoreceptors - detect level of CO_2 in blood by monitor H^+ ion level.

Receptors for pain and other sensory modalities are similar to those in skin, however there exist NO proprioreceptors in viscera and fewer temp. and touch receptors

Pain receptors are distributed in periosteum, arterial wall, joint surfaces and surfaces of viscera.

Stimuli ex:

- Ischemia - No O_2 → anaerobic glyc. → lactate → acidic product → pain.
- Chemical stimuli - damaging substances leak from GIT into peritoneal cavity → pain
- Spasm of a hollow organ - spasm of gut, gallbladder, bile duct, ureters etc cause pain due to mechanical stimulation of pain endings.
- Overdistension of a hollow organ - ex. overfilling causes stretch and consequently pain.

There exsist also organs which are insensitive ex. liver parenchyma & lung alveoli.

Sensations from thorax & abdomen are transmitted by 2 pathways:

① Visceral pathway: pain is transmitted via pain nerve fibers and pain is referred to surface areas of the body. Fibers are C-type, transmitting slow pain. Pain located at a distance from the painful organ.

② Parietal pathway: sensation is conducted directly into local spinal nerves from parietal peritoneum, pleural or pericardium. These sensations are usually located directly over the painful area.

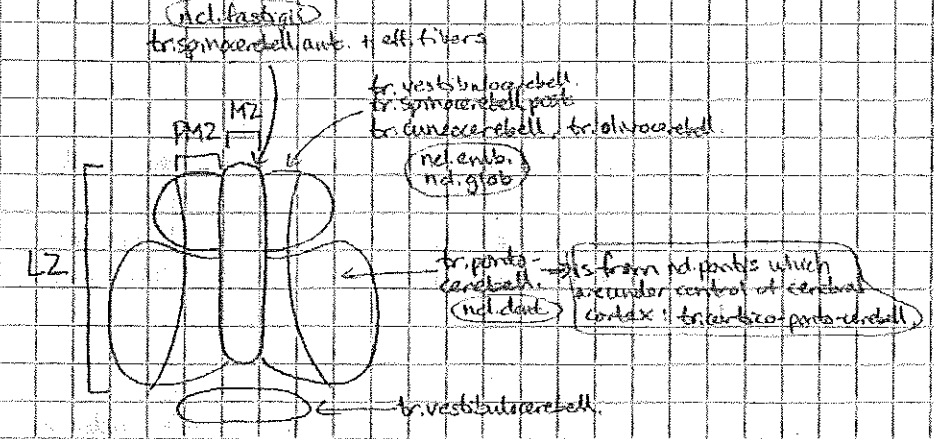
See also pathway of the visceral sensation!

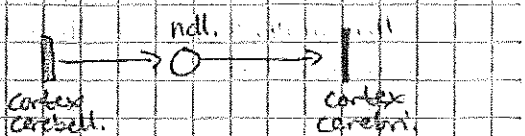
Structural-functional compartments of cerebellum (horizontal & longitudinal divisions)

Situated below cerebrum, behind brainstem. Plays an important role in motor coordination, body position and balance. Consist of vermis + 2 hemispheriae.
Grey matter is arranged as 4 nuclei inside & cortex on surface.
White matter contains aff. + eff. fibers which all pass through pedunculus cerebell. ad pons.
Cortex receives info, then sends it to its nuclei, which sends info to cortex of cerebrum.

(sagit. division) Cortex is divided into:
- medial zone → cover vermis + ncl. fastigii
- paramedial zone → paramedial cortex + ncll. emboliformes + globosi
- lateral zone → lateral cortex + ncl. dentatus

Cerebellum is divided horizontally into: Lobus ant., post. et flocculonodularis.
Separated by fissura prima, horiz. + nodulofloccularis.





is from nd pontis which are under control of cerebral cortex: tr. cerebro-ponto-cerebell.

Cortex cerebelli:
molecular, purkinje, granular layers
(ends axons to cerebell. nuclei!)

General function of cerebellum

It's involved in movements. It corrects and coordinates the movem. and regulate the speed of it.
If lesion occurs in one side of cerebell, the same side of body will be affected = it's called homolateral effect.

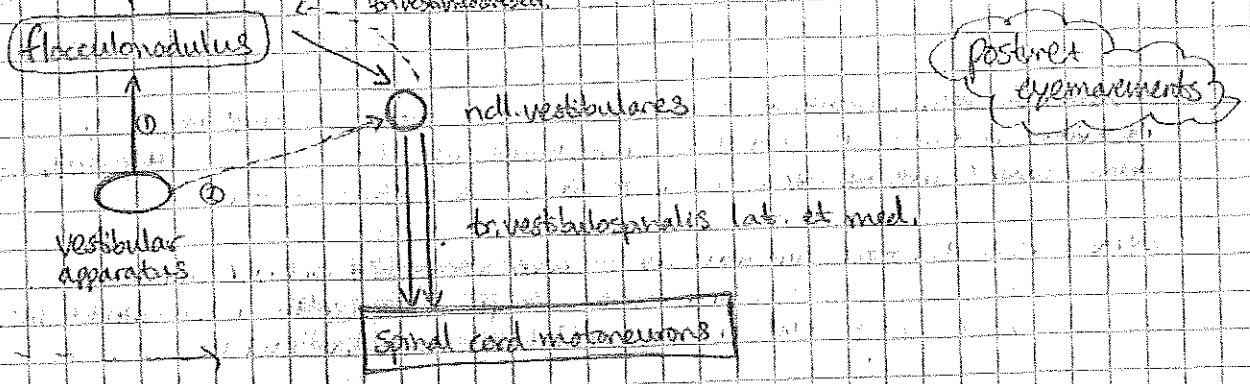
Lesion of vestibular cerebellum (flocculonod.) — result in ataxia (= loss of coordination of muscle movements) of axial muscles without tremor & hypotonia (low muscle tone)

Lesion of spinal cerebellum (M2 + PM2) — result in titivation (= fast rhythmic movements) of head and trunk when sitting and when walking.

Lesion of pontocerebellum (LZ) — hypotonia, decrease of tendon reflexes
asynergie, loss of muscle coordination
decomposition of movement
terminal tremor
defects of speech - dysarthria (staccato)

Phylogenical	Anatomical:	Connections:	Function:
archicerebell.	flocculonodular lobe	ncll. vestibulares	posture & eye movements
paleocerebell.	spinocerebellum (ant. + post. vermis)	spinal cord	progressive movement (eg. walking, swimming)
neocerebell.	pontocerebellum (lat. cortex)	cerebral cortex via ncll. pontis	manipulative movement and speech

Connections of vestibular cerebellum and their contribution to the motor control



Vestibular cerebellum consist of flocculonodular lobe. It recieves signals from vestibular apparatus. Flocculonodulus then sends signals to ndl.vest. and modulate the output of these nuclei.

Ndl.vest. also recieves input directly from vestibapparat.
Ndl.vest. send signals to spinal cord for maintainance of balance via tr.vest.spin lat + med.

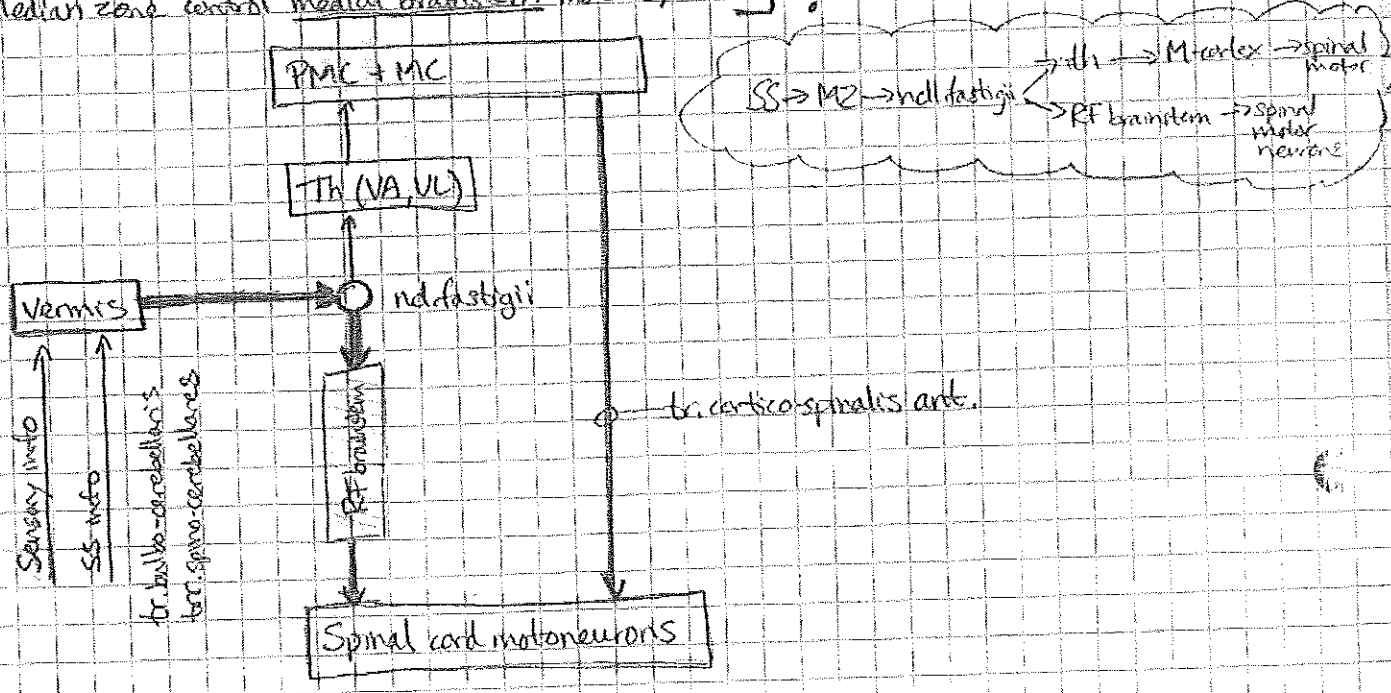
Via tr.vest.spin. lat + med. vestibular cerebellum influence motoneurons for axial muscles and also plays a role in the control of eye movement and their coordination with movement of head.

Connections of spinal cerebellum (median zone) and their contribution to the motor control

Spinal cerebellum contain median zone & paramedian zone of cerebellum. For walking, swimming...

Median zone recieves info to vermis which sends signals to ndl. fastigii, which sends axons out of cerebellum that ends on RF in pons. Through this RF they influence spinal motoneurons.
A small part of axons from ndl. fastigii also goes to motor nuclei in thalamus (VA/VL) which then project to premotorcortex and motorcortex.
Those cortical regions have direct connection with spinal motoneurons via tr. cortico-spinalis ant.

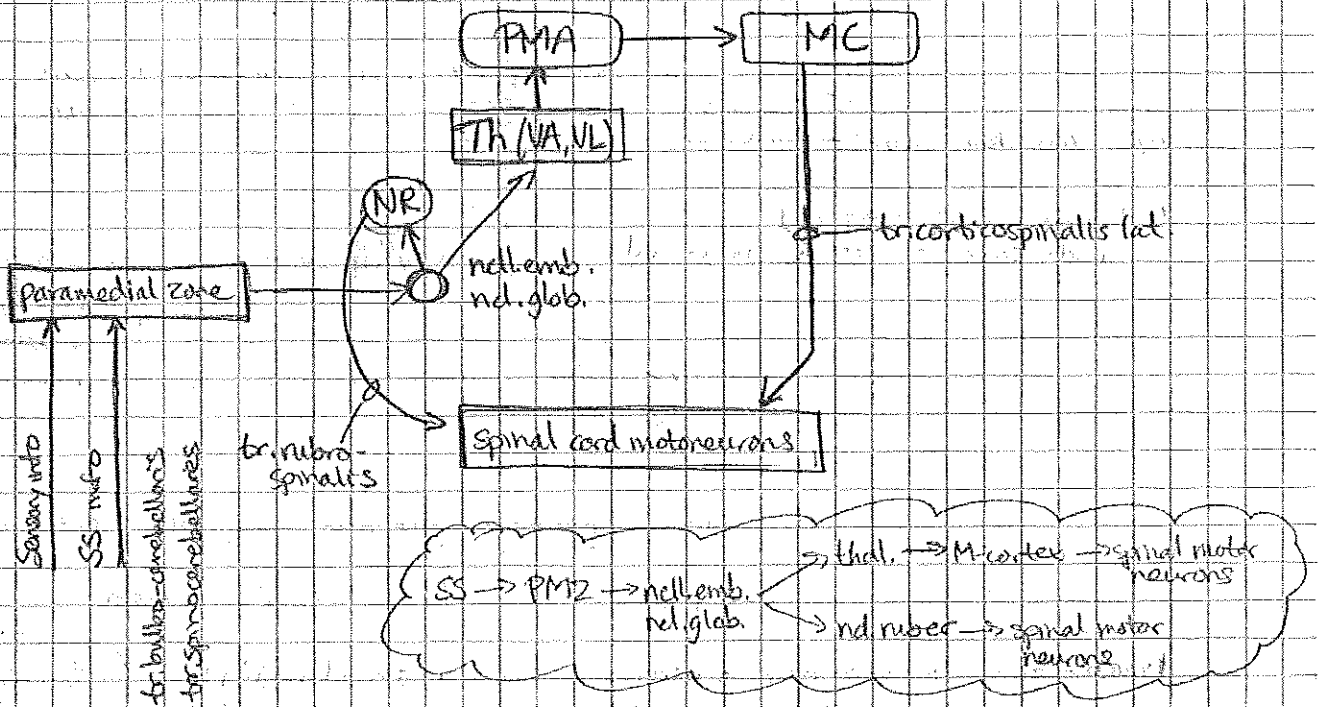
[Median zone control medial brainstem motor system.] !



Connections of the spinal cerebellum (paramedian zone) and their contribution to the motor control.

Paramedian zone: cortex in this zone recieves signals & send them to ncll. emboliformes + ncl. globosus. These nuclei send signals to ncl. ruber (NR) which send axons to lower motor neurons via tr. rubrospinalis.

Signals from emb + glob. can also go to upper structures through motor ncll. in thalamus, which then project signals to premotor area (PMA) of cortex, which sends signals to primary motor cortex (MC), which sends axons in tr. corticospinalis lat.



Functions of paramedial zone: [• control lateral (cortical + brainstem) motor system through ncl. ruber and tr. rubrospinalis] !

• control spinal cord motoneuron activity (distal muscles of extremities) through cortex and tr. corticospinalis lat.

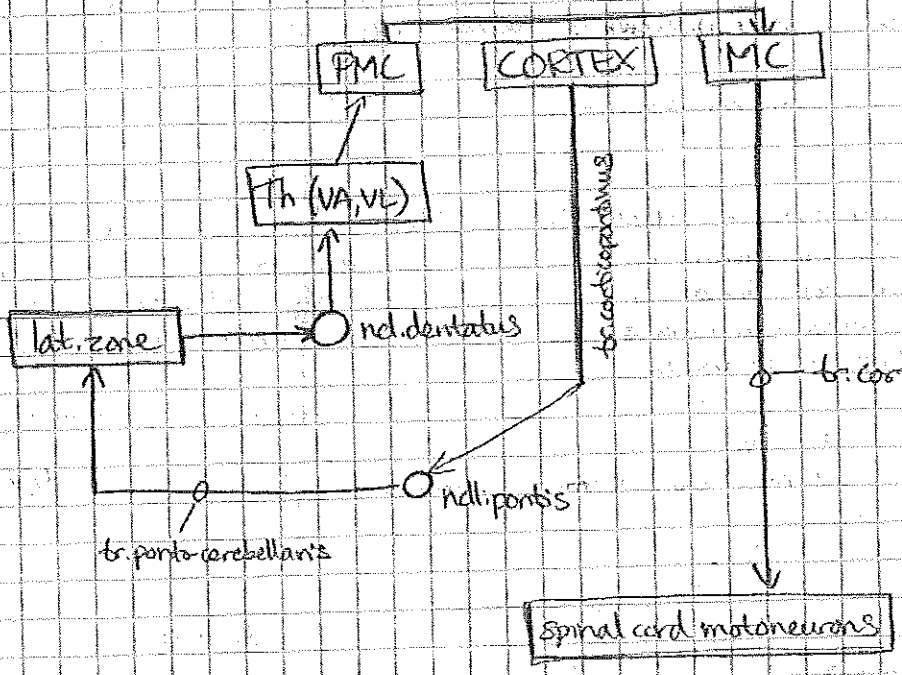
Role of cerebellum in motor control

- Vestibulocerebellum (flocculonodulus)
- Spinocerebellum (M2 + PMZ)
- Pontocerebellum (LTZ)

Connections of pontocerebellum and their contribution to the motor control

Pontocerebellum contain the lateral zone of cerebellum.

Cortex send signals to pontine nell. which then are connected with lateral zone cortex of cerebellum through the pedunculus cerebellares.
Lat. zone elaborate these signals and send axons to nel. dentatus, which send axons to thalamic motor nuclei, which project to premotor cortex (PMC). It will send signals to motor cortex which will then influence spinal motor neurons.



Pontocerebellum is involved in the control of the motor planning and in control of targeted movement. — for speech + manipulative movements
It's also involved in cognition = the solution of problems, linguistics phrasing.
Cognition is not a motor function.
If lesion in this part of cerebellum it not just only result in changes of motor function, but also in cognition.

Cortex → nell. pontis → LZ → nd dentatus → th → M-cortex → spinal motor neurons

The basal ganglia, their afferent, efferent and internal connections

BG
- striatum
  - nucl. caudatus
  - putamen
  - nucl. accumbens
- pallidum
  - external segment
  - internal segment
  - ?

striatum = dorsal striatum + ventral striatum

dorsal pallidum

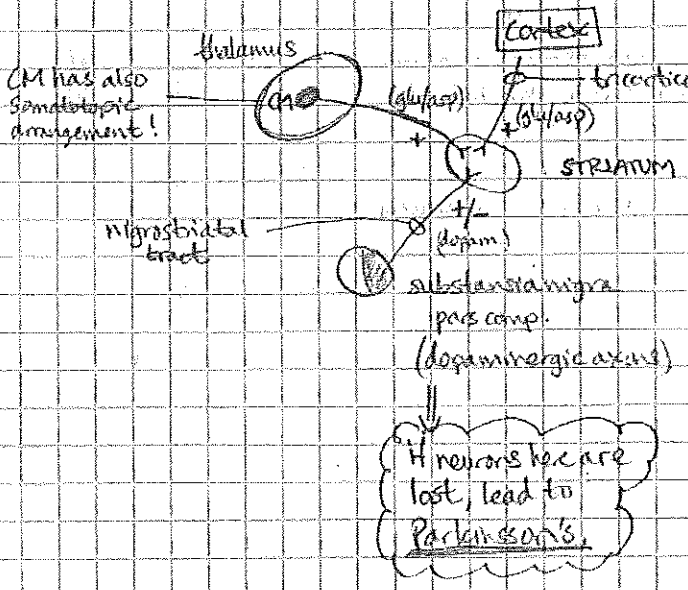
ventral pallidum – has no nuclei (grey matter)

> Grey matter of telencephalon is divided into BG as nuclei inside & cortex on surface

Related structures: substantia nigra → pars reticularis, pars compacta

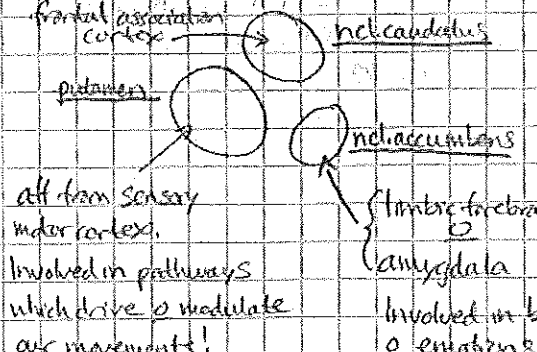
nucl. subthalamicus

Afferent BG → Striatum will recieve all impulses, mainly from cortex and central (CM) medial nucleus in thalamus. They use glutamate or aspartate as neurotransmitters. In pars compacta of substantia nigra, neurons will send axons to striatum which inhibit or activate neurons in striatum. Axons contain dopamin which is released in striatum.
Neurons in striatum are inhib./activ. depending on what receptor they have. If they have dopamin D1-receptor it will ↑ its activity.
If neuron has dopamin D2-receptor it will become inhibited.



If neurons here are lost, lead to Parkinson's

The different parts of striatum receives different axons from cortex:

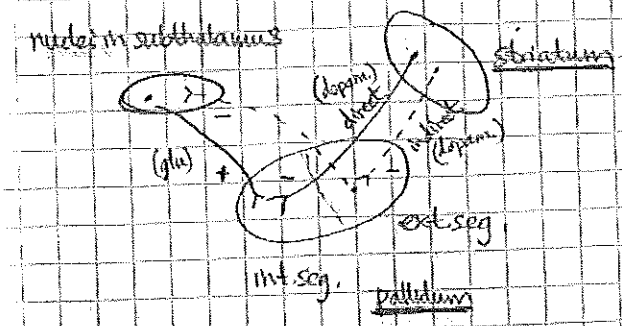


aff. from sensory motor cortex. Involved in pathways which drive & modulate our movements!

Involved in behavior & emotions!

Intrinsic BG – connections btw striatum & pallidum. Can be direct or indirect.

Pallidum is divided into internal/external segments.
In striatum we have 2 diff neurons. Neurons with direct connection with internal segment and neurons with indirect connection with internal segment



DIRECT
neurons with direct connection to int. seg. contain dopamine & inhibit neurons in int. seg.

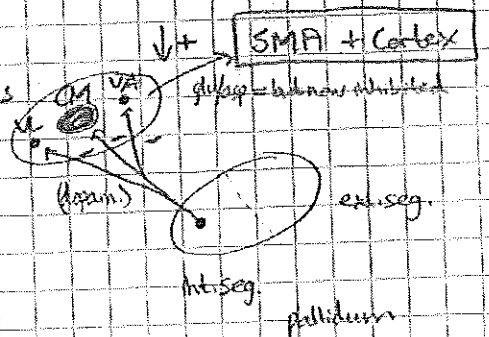
INDIRECT
Nucl. subthalamicus is connected indirect with striatum.
Neurons in ext. seg. is inhibited by neurons in striatum. This makes some neurons in subthalamic nucleus to become inhibited = double inhibitory function!
When neurons in subthalamic nucl. inhibited this cause some neurons to become activated which are connected with int. seg. of pallidum. They use glutamate as transmitter.

(+ Hierarchic organisation...
Role of BG in motor control) + sensory motor loop!

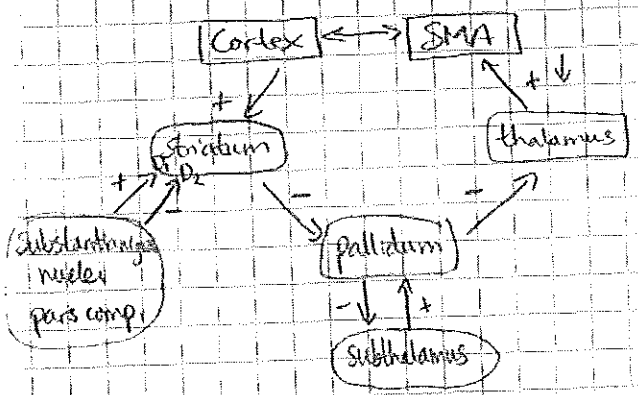
Efferent connections of BG – connections for sending signals outside of BG.

Internal segment of pallidum contain inhibitory neurons which are connected with thalamic nuclei. Nuclei in thalamus (VA, VL) usually project signals to cortex and excitate neurons there (because axons use glutamate) but when axons from pallidum inhibit the neurons in thalamus they can't send any signal to cortex.

Summarize: neurons in pall. inhibit neurons in thal. & also in supplementary motor area (SMA) so neurons in cortex will decrease their activity.



General connections of BG:



4 loops of BG:

Sensory motor loop – for planning of arm movement
Start in S. cortex, end in supplementary motor area.

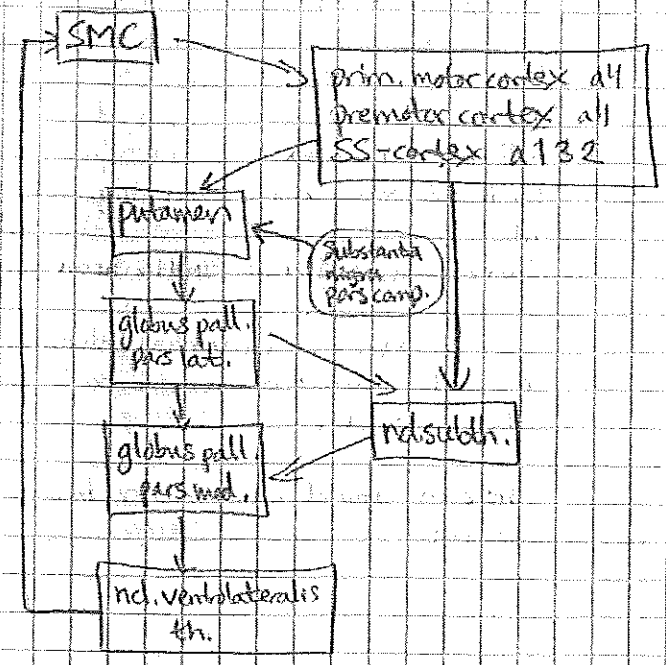
Association loop – for space memory.
Start in premotor cortex, end in prefontal cortex

Limbic loop – for motor expression of emotions, ex. laugh, sad, angry.
Start in amygdala, ends in cortex of g. cinguli.

Oculomotor loop – Ha för saccadic eye movements
Start in premotor cortex, end in frontal visual field.

Four basic functional loops of BG

Sensory motor loop — Function: control of movement and their preparation.

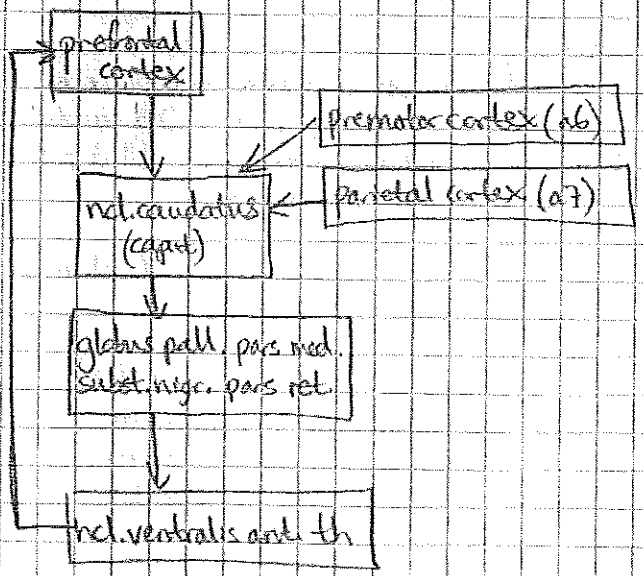


Putamen recieve afferentation from SS-cortex etc..
Pallidus connects with thalamus to send signals back to supplementary M-cortex. In this loop BG are involved in control of movement and their preparation.

Cortex and globus pall. are also connected with subthalamic nuclei.

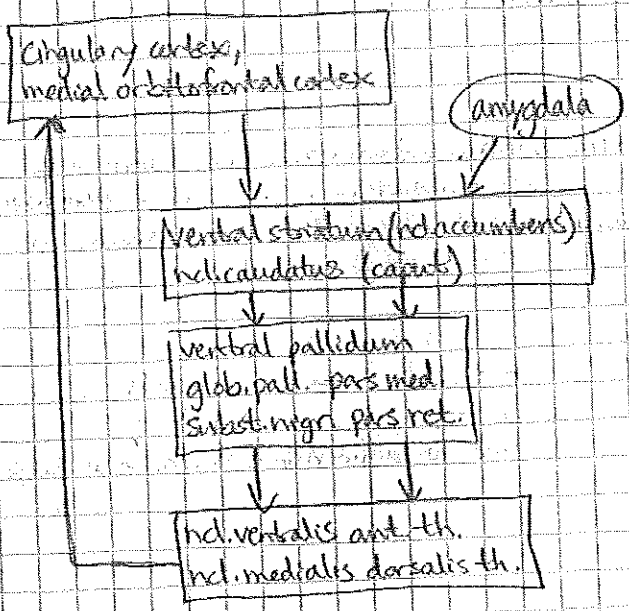
And substantia nigra is connected to putamen.

Association (prefrontal) loop — Function: space memory



This loop is involved in space memory. The loop starts in premotor and parietal cortex, project to ncl. caudatus which project to globus pallidus and to thalamus and the loop ends in prefrontal cortex.

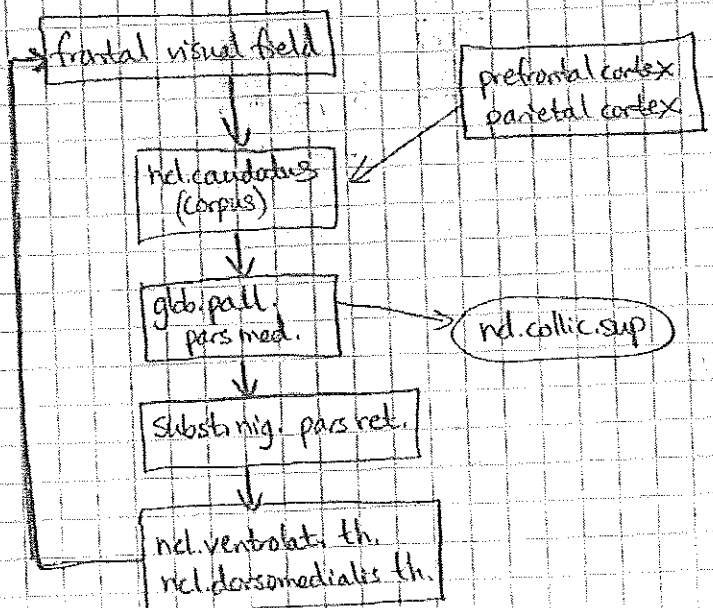
Limbic loop – Function: motor expression of emotions aggressive or submissive attitude gesture, laugh



This loop begins and ends in cingulate gyrus cortex and medial orbitofrontal cortex.
The loop receives input from amygdala which send signals to ventral striatum (nd.accumbens) and to the head part of caudate nucleus.
Info is processed in ventral pallidum, glob.pall. & substt. nigra and sent to thalamic nuclei.

Here info project into cortex & loop is closed.

Oculomotor loop



Begins in prefrontal and parietal cortex, they project to nd.caudatus and info is processed in globus pall. and substantia nigra.

From here signals go via thalamus to frontal visual field.

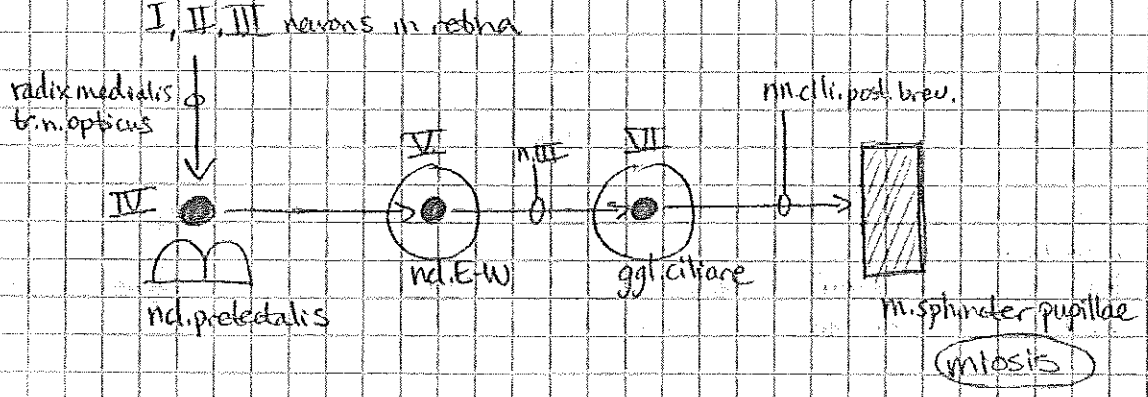
Globus pall. is also connected to nd.collic.sup. to participate in control of saccadic eye movements.

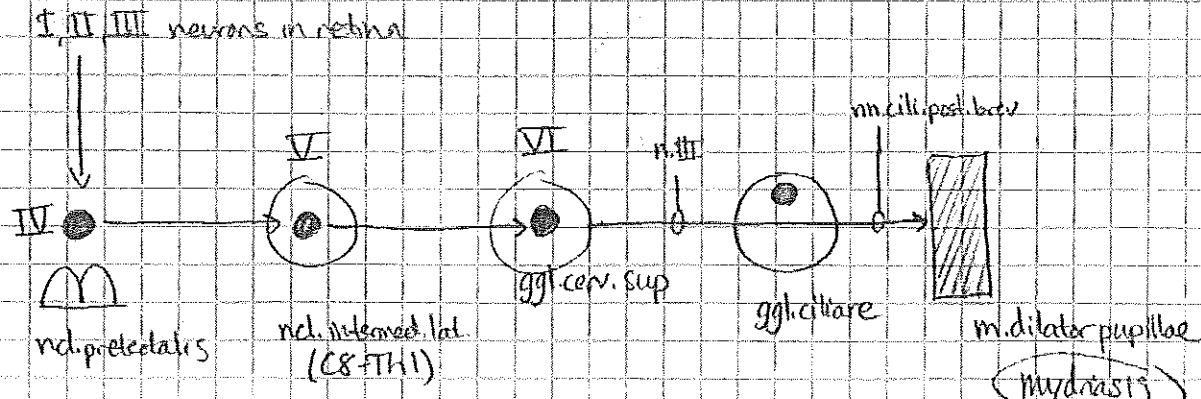
Pathways for miotic pupillary reflex & Pathways for mydriatic pupillary reflex

I-III order neurons are present in retina. Rods/cones → bipolar → ganglionic → axons in tr.opticus and travel in radix med. to ncl.pretectalis which have IV order neurons.

For m.sphincter pupillae – IV are connected with ncl. E-W (parasymp. nucleus) which contain V neurons. It sends preganglionic fibers in oculomotor nerve to ggl.ciliare. Here are VI neurons which send postganglionic in nn.ciliares post.brev. to m.sphincter pupillae = miosis

For m.dilator pupillae – IV are connected with symp. neurons in ncl. intermediolateralis present on spinal cord level (C8-Th1). They are V. They send axons in symp. trunk which reach to sup.cervical ggl. Here VI neurons send postganglionic inside n.oculomot. & through ggl.ciliare (without synapses) and through nn.cil.post.brev. to innervate m.dilator pupillae = mydriasis



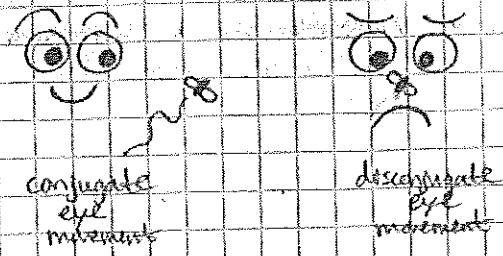


How we control our eye movements

For sharp vision we need to concentrate light on fovea centralis. We have only 1-2 degree of vision field.
To keep object on fovea we need some coordinations of 12 extraocular muscles.

We recognize 2 movements of eyeball:

- Conjugate movements – when we simultaneously move both eyes in same direction, ex when following an object
- Disconjugate (vergent) movement – when we follow an object which move toward us or from us.



We have many groups of cortal systems for our eyes:

- Pathways which control the coordination of eye movements when we move our head.
  - Vestibular-ocular pathway – is an adaptive system, it use info from vestibular system to stabilize a picture.
  - Opto-kinetic pathway – stabilize picture on fovea centralis by following the object with visual system
- Slow pursuit system – adaptation of eye and object movements. Ex when drive car.
- Fast saccadic movements – fast stereotypical movements, we can scan the surrounding by this system to find an object.
- Vergent movements – both eyes remain upon an object from different positions.

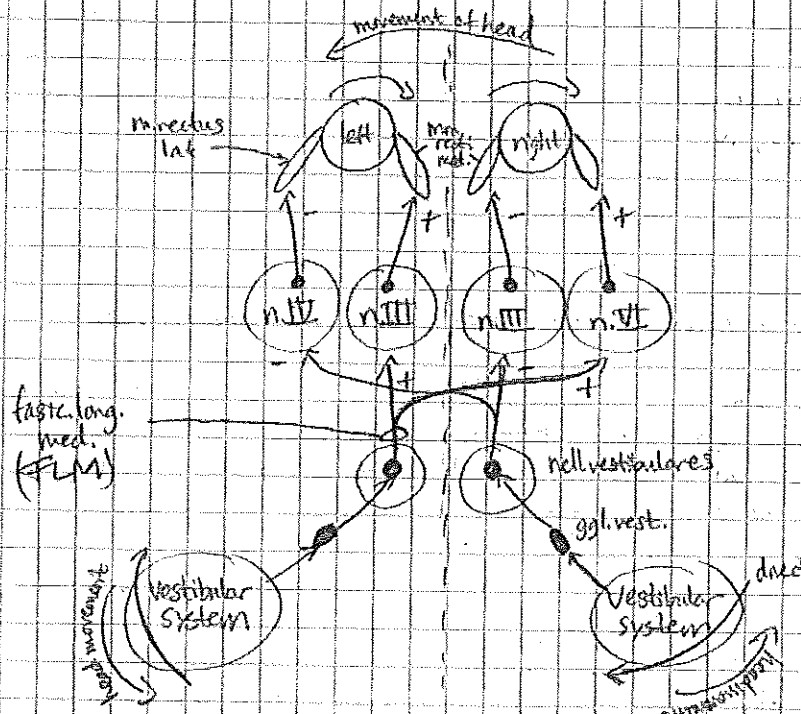
Pathways for vestibulo-optic reflexes

- for horizontal movement:

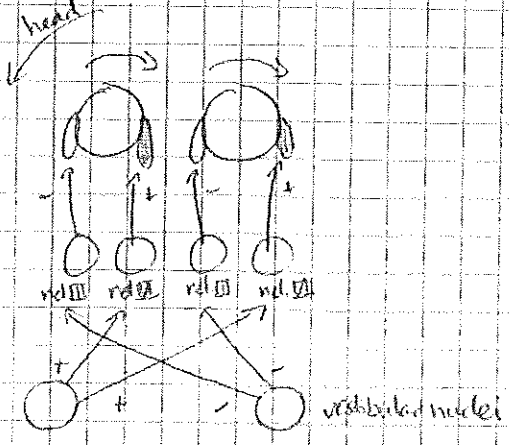
When we move our head to ex. left side but we want to fix eyeballs to an object, eyes must move the other way (to right). Eye muscles on right side of eyes will be stimulated by motor neurons to contract, but on the left side of eyes muscles must be relaxed. This is done by the inhibition of their motorneurons.

This inhibition/stimulation is done by the vestibular nuclei which receives info from vestibular apparatus.

As a cause when we move our head signals from vestibular system will go to nd. vestibulares and they will, in turn, send off inhib/stim. signals to corresponding motor nuclei. The signals will be sent in fasc. long. med. (FLM)



← Compare q. the vestibular pathways, scheme & description!

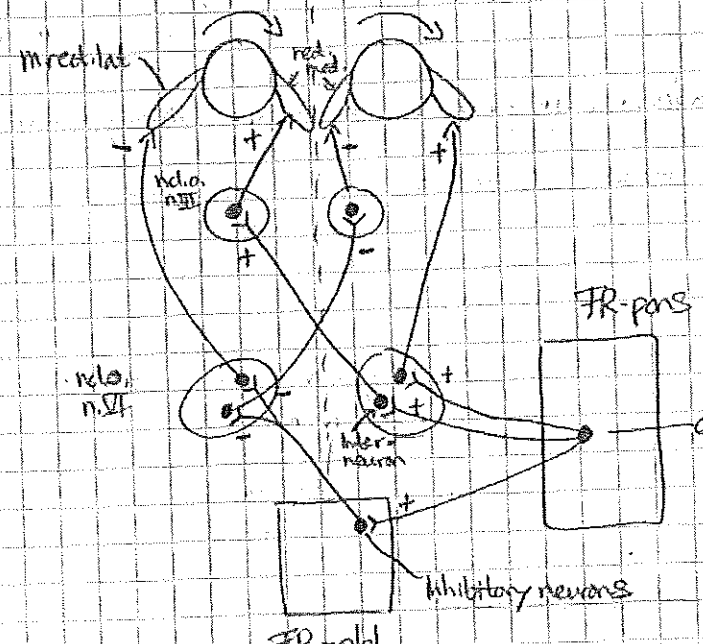


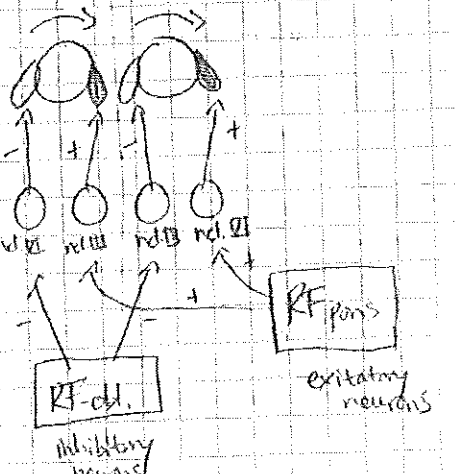
Pathways for control of slow eye movements = optokinetic reflex?

When we follow an object which move to the left or the right, we need to coordinate the eye muscle movements.
If we look to right, neurons which activate motor neurons to right side eye muscles are stimulated, and at same time neurons to left side are inhibited. So left muscles relax.

In FR of pons we have exitatory neurons & in FR of obl. we have inhibitory neurons.
When look to right, exitatory neurons stimulate motor neurons in ncl.o.n.III to contract m.rectus lat. on right side of eye. And at same time they also send exitatory info via interneurons in ncl.o.n.VI which stimulate neurons in ncl.o.n.III to contract m.rectus med on left side.
⇒ eyes want to move to right side.

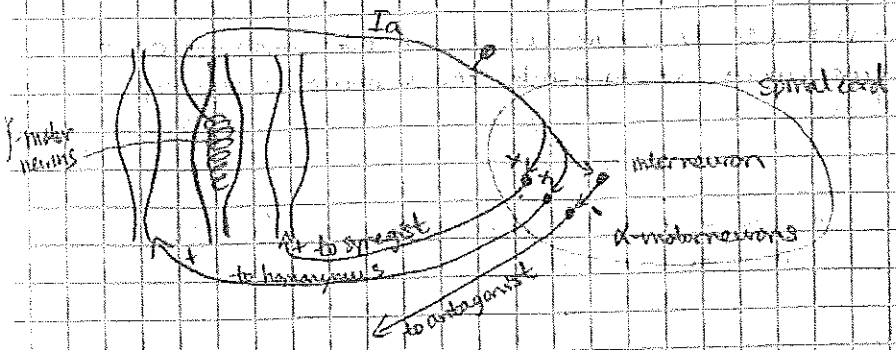
But for eyes to move to right side, we have to relax m the muscles which are on the left sides of eyes.
Therefore the exitatory neurons (in FR on right side) also send some axons to FR in obl. and activate some inhibitory neurons. These inhibitory neurons inhibit the motor neurons in contralateral ncl.o.n.VI and also inhibit the interneurons in ncl.o.n.VI which usually exitate the neurons in ncl.o.n.III. Thus the left side muscles are inhibited and relax.





Reflexes in motor control

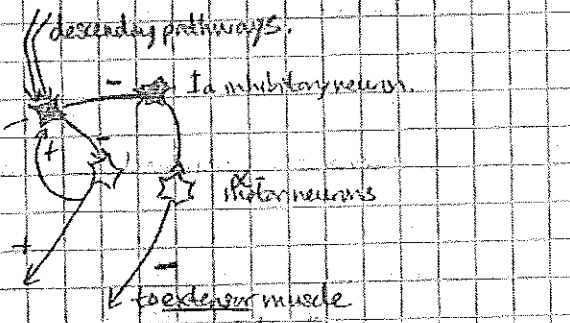
Proprioceptive spinal reflex = myotatic reflex



γ motorneurons innervate the muscle spindles. Afferentation is carried in Ia fibers to spinal cord where they stimulate α-motoneurons to cause contr. in synergist muscles or in the same muscle (homonymous contraction).
The Ia fibers can also stimulate interneurons which then inactivate the α-motorneurons which innervate the antagonist muscle, thus making it relax.

Renshaws cells

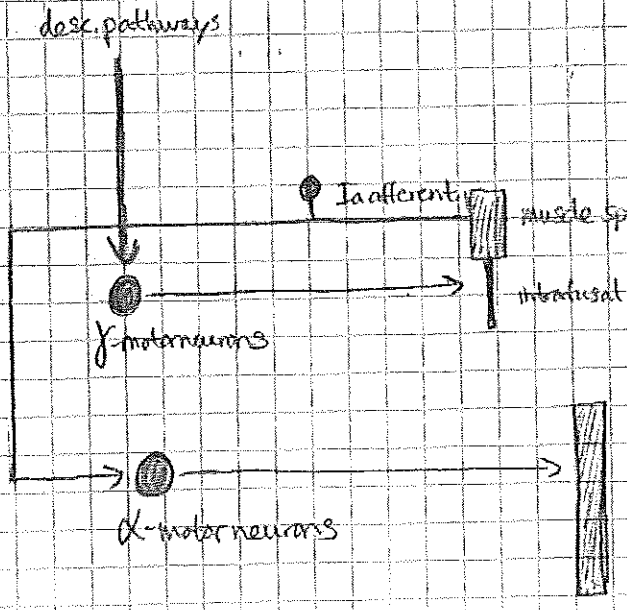
Are a type of inhibitory interneurons in ant. horn.
They receive axons from a motor neuron and inhibit it, it's like a self-inhibition.
Renshaws also have contact with Ia-inhib neuron. Renshaws will inhibit it so that the antagonist muscle can contract.
R-cells are also under control of descending pathways which can stimulate/inhib. it.



This myotatic reflex can be tested, for example by testing the knee jerk reflex.
It's used to test if spinal segments are intact in L2-L4.
By hitting tendon you passively stretch the muscle and this stimulate stretch in muscle spindle. Ia will thus stimulate α-motoneurons which will cause contraction of quadriceps.

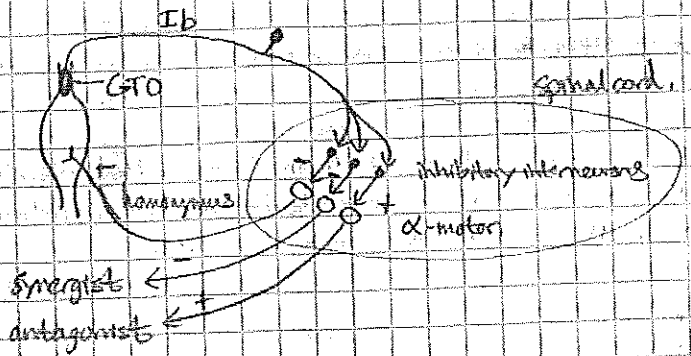
The gamma loop

Muscle spindle with intrafusal muscle fibers are innervated by Ia fibers which stimulate α-motor ⇒ cause contraction of muscle.
Intrafusal fibers are adjusted by γ-motor neurons which are controlled by descending pathways.



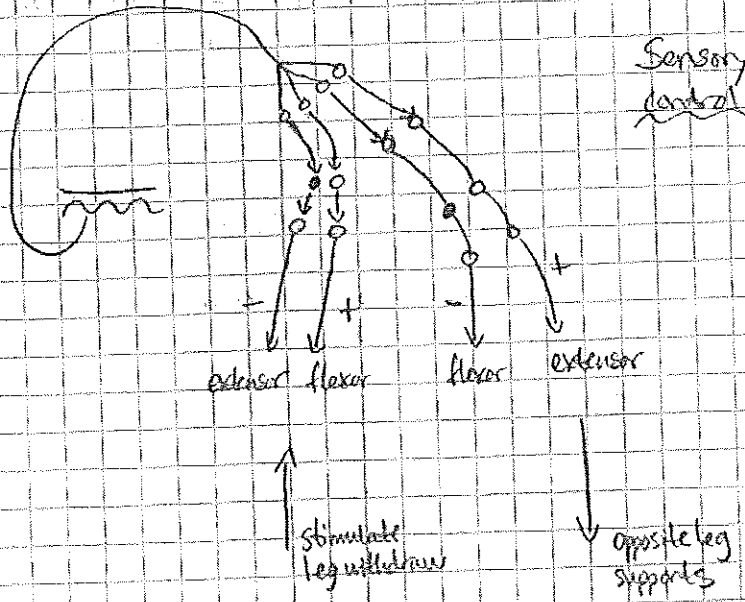
Golgi tendon organ reflex

Golgi are also encapsulated by c.t. capsule, but inside we have clusters of collagen fibers and between them are dendritic zones of Ib fibers.
Golgi are innervated by Ib-afferent fibers. They follow the spinal nerves and end on inhibitory interneurons in spinal cord, which in turn inhibit the α-neurons.
Thus ↑ activity of Ib lead to ↓ activity of α-neurons of same muscle fiber!



Flexion-withdrawal and crossed extensor reflex

Afferentation comes from skin → go in common aff. axons to spinal cord & end on interneurons. We have both − & + interneurons. α-motoneurons of flexor are activated by excitatory interneurons and inhibitory neurons inhibit α-neurons of extensor.
Ex. When we walk, skin of foot makes this reflex happen.



Sensory information necessary for the control of movements

3 motor systems for the control of movements:
- Medial
- Lateral
- 3rd motor system

To control our movements we need proprioception + afferentation from somatosensory system (skin).

Resting potential of the neuron

If we place one microelectrode inside a cell and another into the ECS, we will detect a small electric voltage. The magnitude of the voltage of several millivolts. In nerve cells we will measure at resting conditions a voltage of about -60 mV (and on a muscle cell around -90 mV). This means that the interior of the resting cell is ca 60 mV more negative than the exterior.
Smooth muscle cells have a -55 mV and RBC -9 mV.

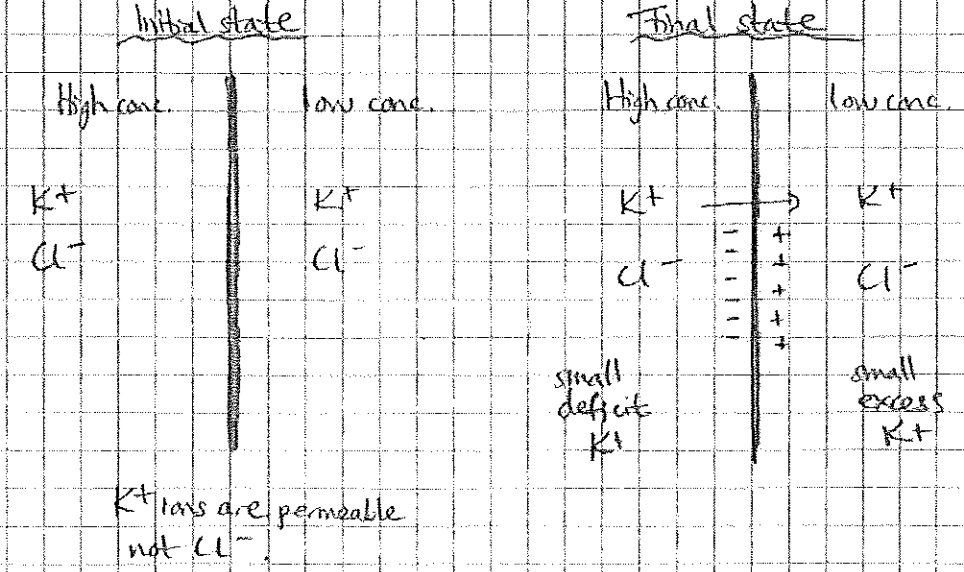
This membrane potential (= the voltage difference between the interior o exterior of cell) arises because the composition of ions on either side is different, mainly Na^+, K^+, Cl^- o Ca^{2+}.

The lipid bilayer is usually impermeable for electrically charged particles, but ions travel through specific ion channels and ion pumps to the other side, by active transport. These carrier proteins help to maintain the uneven distribution of ions.

Conc. of K^+ ions inside cell is high
Conc. of Na^+ and Cl^- ions outside cell is high.

If a non-zero permeability of the membrane for these ions would exist their conc. would gradually become equal on both sides of membrane.

Lets imagine a system composed of a membrane with same electrolyte on both sides, but with different conc. Ex. KCl which dissociate into K^+ and Cl^-.
The membrane is only permeable for K^+ ions.
K^+ will try to equalize its conc. on both sides, so K^+ will start to move from the higher conc. to the lower conc.
However, the problem is that the ion with opposite charge (Cl^-) can't diffuse together with the K^+ ions because membrane is not permeable for Cl^-.
The flow of K^+ will therefore be stopped by an electric field (a potential difference) generated as a result of the uneven distribution of the ions on the membrane.



The membrane potential has 2 functions:

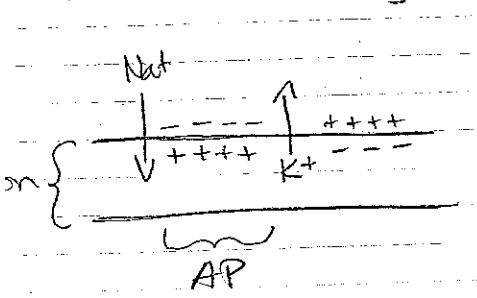
- Allow cell to function as a battery, it provide power to drive various transport processes across the membrane.
- And in electrical excitable cells like neurons it's used for transmitting signals. The electrical impulses produced by such cells are called APs.

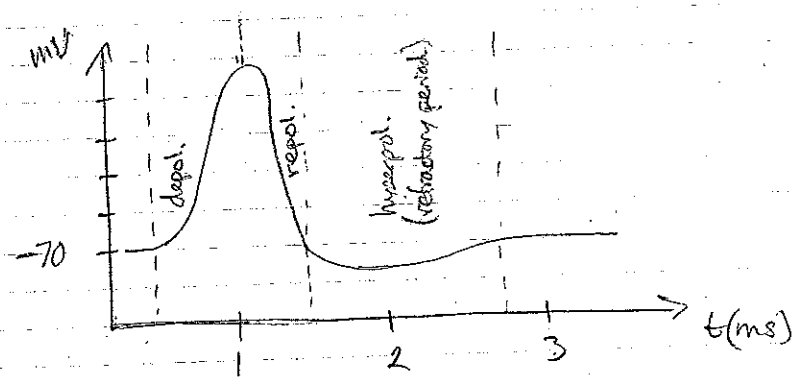
Ionic basis of membrane potential changes

The quick change of the membrane potential is called an action potential (AP).
It's possible in cells with excitable capacity, like neurons.

The process starts with the opening of Na^+ channels. Their permeability will increase about 500 times. A lot of Na^+ ions will rush into the cell and make it more positive on the inside. The membrane potential will be rapidly changed to a positive value.
This phenomenon (when Na^+ rush into cell) is called depolarization.

Almost simultaneously the permeability of K^+ channels are increased, K^+ will flow out from cell and thus stop the rapid change of the potential. This is called repolarization. K^+ channels will stay open for a little bit longer time which will lead to potential values to drop even lower than the resting values. This is called hyperpolarization.
The time interval during which membrane is hyperpolarized is called refractory period.





Spreading of membrane potentials. Length and time constant of the membrane.

Stimuli from dendrites are gathered at hillock, when reach a special level an AP will be formed! Na^+ channels open if the value of resting membrane potential changes by at least 15 mV in the positive sense, this is called <u>local response</u>.

When the channels are opened they allow inward flow of Na^+, which results in a further rise in membrane potential. This cause more channels to open and more local responses. ↑ rise in membrane pot. This process proceeds until all channels are opened on a limited <u>local area</u>. The magnitude of local responses depends on the magnitude of stimuli.
The AP belongs to the phenomena "all or nothing". It either doesn't originates or it does originate, and then it always has the same magnitude. If magnitude of local response reach −55 mV we call it a <u>threshold</u>, an AP will form!
The AP always travel in one and same direction. This is due to the hyperpolarization at places through which the AP has already passed. Hyperpol. causes a drop in the sensitivity of the membrane to another electric impulse, thus AP only travel to places where it has not been before. It takes a time of several milliseconds after the AP has passed to restore the orginal resting membrane potential.

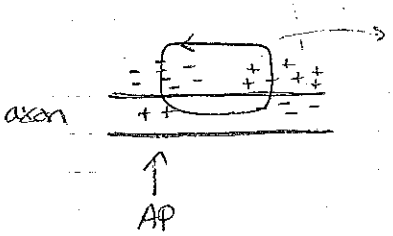
AP occurs in several types of excitable cells, including neurons, muscle cells, and endocrine cells. In neurons they play imp. role in cell-to-cell communication. In other cell types APs activate intracellular processes. Ex. in muscle cells AP is the first step in the chain of events leading to contraction. In β-cells of pancreas, AP provokes release of insulin.

The rate of propagation of the AP is diff. in diff. nerve fibers. It depends if it's myelinated or not.

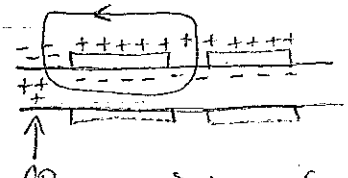
In non-myelinated fiber, propagation = 0,5 m/s
In myelinated fiber = 120 m/s.

Myelin insulation is interrupted at intervalls of ca 1 mm. The gaps are called <u>nodes of R</u>.
Local current = the transfer of ions along the opposite sides of the membrane.
The AP in the nodes of R. initiates local currents that can't be manifested on the membrane until the next gap. AP will "jump" between the nodes = <u>saltatory conduction</u>.
Myelination <u>speeds up</u> propagation & demand <u>less energy</u>.

<u>Conduction of AP:</u>

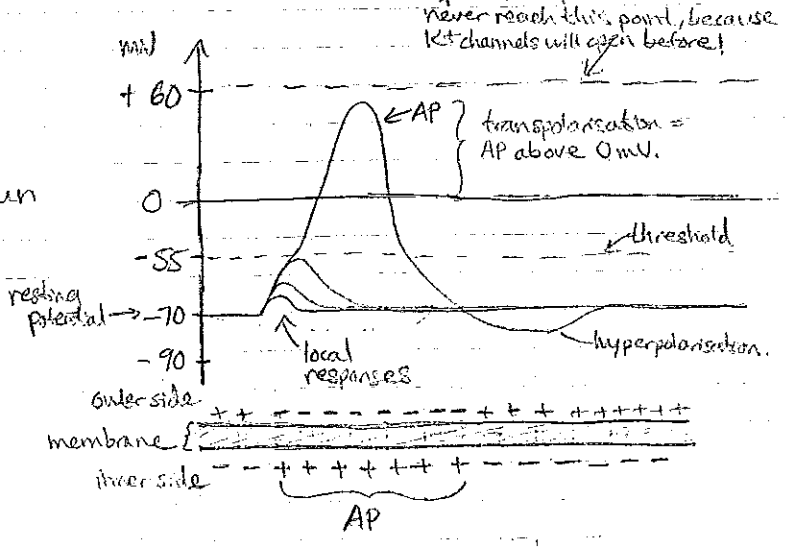


An electrical current loop will be created. It will run through axon.



If axn has myelin sheath, loop looks like this.

AP ⟹ jumps from one node of Ranvier to other = saltatory conduction
The thicker the myelin, the faster signal!



Central nervous structures that control the autonomic nervous system, their description and connections.

There are some structures in CNS that control the structures of ANS.
The structures are:

- Nuclei in hypothalamus
- Amygdala nuclei
- And neurons in brainstem: (induced in coordination of somatic and autonomic answer to behavior, defensive reaction to preganql. neurons.)
  - Periaqueductal grey (PAG) = grey matter around mesenceph.
  - Ventral tegmental area (VTA) } in tegmentum
  - Dorsal tegmental nucleus (DTNd) }
  - Solitary nucleus

These structures influence preganglionic parasymp. and symp. neurons.

- From cortex in frontal lobe signals will go to RF by the way of tr. cortico-reticularis, and then by tr. reticulo-spinalis to influence preganql. neurons.
- From hypothalamus signals will be sent through tegmentum before reaching the preganql. neurons they influence. Two ways are possible: tr. hypothalamo-tegmentalis and tr. mamillo-tegmentalis.
- Limbic forebrain is also involved in the control of ANS. Signals will go through fasciculus long. dors. (FLD) o dorsolateral tegmentum.
- From amygdala signals will run through hypothalamus and PAG to lower pregang. neurons.

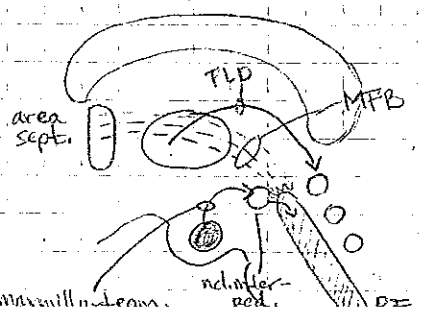
There are 3 main descending pathways which the signals can travel in to reach lower structures:

- Tr. mamillo-tegmentalis
- Fasciculus long. dors. (FLD)
- Medial forebrain bundle (MFB)

Mammillo-tegmental tract → from mammillary body, terminate in nd. interpeduncularis (it's an unpaired nucleus located in fossa interped.). From here signals go through RF and influence pregangl. sympathetic neurons in spinal cord.

FLD → go from hypothalamus to nuclei in brainstem which contain pregangl. parasymp. neurons. Ncll. parasymphaticus nn. III, VII, IX, X.

MFB → white matter comming from septal area (part of limbic forebrain). White matter pass through hypothalamus and is connected with RF. From RF signals is sent futher to influence/modulate pregangl. neurons of symp. neurons in spinal cord.



Responses of effector organs to autonomic nerve impulses

Hypothalamus can be divided into ant. & post. hypothalamic nuclei.

Nuclei of ant. hypothalamus (bla. ncl. preoptic & ncl. supraoptic)
Stimulate parasymp. fibers – mainly in vagus, therefore they're called vagotonia.

Stimulation of ant. hypothalamus results in:

- Constriction of pupilla
- ↓ heart beat & BP
- dilation of skin arteries
- ↑ of peristaltic movement, motility & secretion of GIT

Nuclei of post. hypothalamus (bla. ncl. mammilaris & ncl. hypoth. post.)
Stimulate symp. fibers.

Stimulation of post. hypothalamus results in:

- Dilation of pupilla
- ↑ heart beat & BP
- constriction of skin arteries
- ↓ peristaltic...
- hair erection...

Amygdala = located in temporal lobe on medial side of hemispheres.

Amygdalar nuclei are divided into 3 groups:
- Basolateral group. – phylogenetically younger
- Central nucleus.
- Corticomedial group. – phylogenetically older

Primary function = control of behavior during fear & anxiety.
Other functions = control of motor activity, intake of food, sexual behavior, cardiovascular & endocrine mechanisms, memory, and other cognitive functions.

If do a PET-scan on murderers when they watch horrible films, amygdala will be "silent".

Afferentation of amygdalar nuclei
Nuclei in amygdala receives afferent signals from subcortical + cortical structures to basolateral group.

Subcortical signals = imp. during childhood, they are related to memories of anxiety situations.
Afferentations from subcortical structures induce phobias, ex. claustrophobias or fear of height.

Cortical signals = signals from frontal cortex & temporal cortex. All sensory + SS into which are elaborated by these cortexes are, by some way, connected with amygdala.

Efferentation of amygdalar nuclei
Signals from amygdala to other structures (efferentation) is sent in 2 ways:
- Via stria terminalis, or
- Via ventral amygdalofugal fascicle

Stria terminalis – goes from central nucleus to:
- area septalis – involved in anxiety & fear.
- hypothalamus – then further into PLD to neurons of parasymp. ncll. They drive heart activity, which will explain why you can loose consciousness when look at blood.
- nerve fibers can also go to Medial forebrain bundle (MFB) and then into central tegmental tract.

Ventral amygdalofugal fascicle – axons from amygdala goes in this fascicle to:
- PAG – involved in stress analgesia.
- Ventral striatum – excitate ncl. acc.
- Ncl. accumbens. – significant structure in drug addiction.

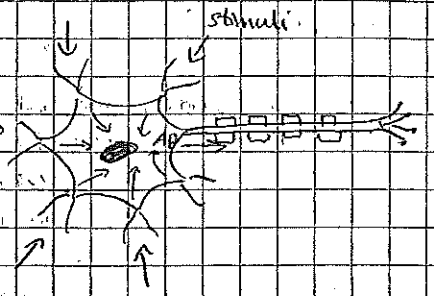
Temporal summation of membrane potentials

When a neuron recieves excitatory and/or inhibitory inputs at same time it "adds" the inputs together. If the excitatory inputs are greater it will result in generation of AP. This addition of inputs is called summation.

We distinguish between 2 summation types:

- Spatial summation

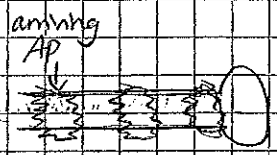
Stimuli from many dendrites are gathered at hillock and when reach a special level an AP will form.

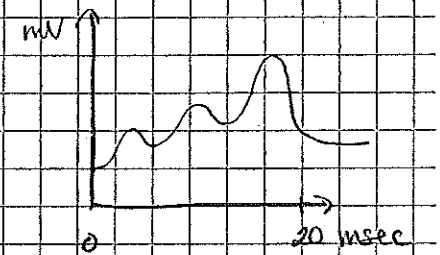


- Temporal summation

Occurs when two or more APs are sent through axon almost simultaneously.
Before the first AP is finished the other AP arrive and they will fuse. The second AP will add its amplitude to the first AP.

The neuron keep firing.





Local APs follow shortly after one another with delays within 5-15 ms. Are fused.

Excitatory and inhibitory postsynaptic potentials
Excitatory and inhibitory neurotransmitters

In which sense the synapse will act is determined by the chemical nature of the neurotransmitter and on its interaction with the postsynaptic membrane.

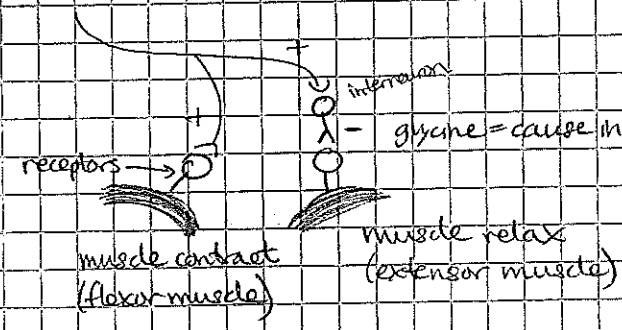
Excitation mediators = glutamic acid (in CNS) or acetylcholine (in neuromuscular junctions & CNS).

Both substances act as ligands: They bind to the protein of sodium channels. The channel will open and Na^+ will go into cell. The membrane pot. will change in the pos. sense, the so called excitation postsynaptic potential. This is not an AP, only a change in membr pot.
When multiple EPSPs occur on a single point of the postsynaptic membrane they will fuse to one large EPSPs and when reach a special treshold the postsynaptic neuron will fire an AP.

Inhibitory mediators = γaminobutyric acid (GABA) or glycine.

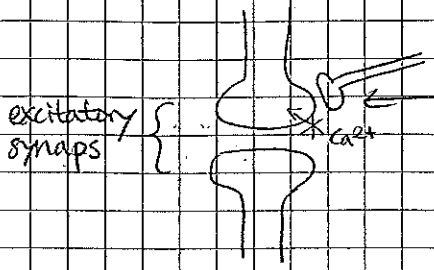
It acts as a ligand to chloride channels. Cl^- will go into cell and this will make a drop in membrane pot.; the so called inhibition postsynaptic potential.
This potential will decrease the change of an AP to be formed.

This is the function of antagonists muscles:



Presynaptic inhibition and posttetanic potentiation

Presynaptic inhibition



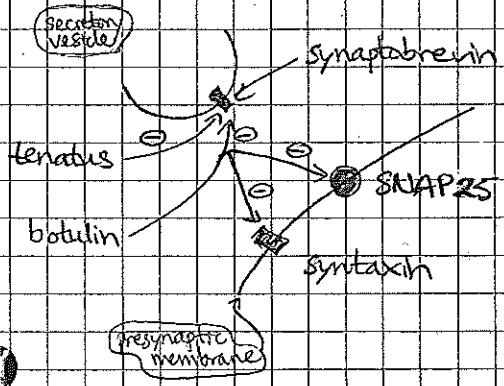
Presynaptic inhibition
The transmitter is GABA.
It opens Cl^- channels on presynaptic neuron.
Cl^- makes AP ↓.

Because Cl^- go into cell, less Ca^{2+} channels are opened and Ca^{2+} don't go into terminal.
⇒ Less transmitters in excitatory synaptic cleft is released!

Strychnin – block this mechanism. If this mechanism is blocked it will cause spastic paralysis like tetany. Person will die.

Tetanus and botulin

Some bacterias can block some proteins in the synapse and cause disease.



Synaptobrevin = is a protein in the secretory vesicle which contain neurotransmitters.

SNAP25 = is a protein in presynaptic membrane which help synaptic vesicle + plasma membrane together.

Syntaxin = is also a protein taking part in fusion of membrane + vesicle.

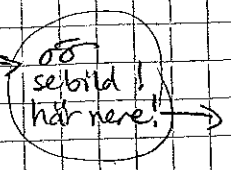
Tetanus = a disease caused by clostridium tetani. This bacteria will enter damaged tissue and produce tetanus toxin (tetanospasmin). This toxin will bind irreversible to synaptobrevin receptors and block them. No neurotransmitters will be released into synaptic cleft. GABA + glycin are inhibitic neurotransm. If not released, can't inhibit. Muscle will not stop contracting!
⇒ muscle rigidity and spastic paralysis.

Botulin = a disease caused by clostridium botulinum. Intake by food. The toxin produced by these bacteria bind to all 3 receptors and cause vesicles not to fuse = no acetylcholine is released into synaptic cleft at neuromuscular junctions. = no contraction!
Acetylcholine is the transmitter btw nerve + muscle. If it's inhibited it causes flaccid paralysis of muscles
Botulin is sometimes used to treat muscle spasms. Ex. achalasia = insufficient relaxation of muscle in distal part of oesophagus ⇒ botulin ⇒ it will dilate.
Botulin is also used to treat wrinkles, the tradename is Botox. It paralyse muscles where it's injected ⇒ cause wrinkles to disappear!

- tetanus: stop secretion of glycin & GABA. Mortality is 100%. To prevent: vaccination.
- Curare: block the receptor for acetylcholine. Skeletal muscle paralyse → breathing stops! If do mouth to mouth in 15 min, curare will disappear & person will live!

Neuromuscular junction – structure & function

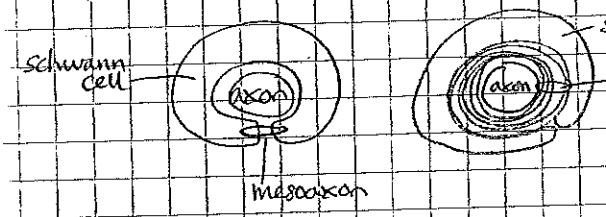
Is a special type of a chemical synapse. It differes from the other types by its size and a more complicated structure.
It is the termination of a motor nerve axon and the muscle.
Activity of this synapse cause contraction of muscle fiber.

The chemistry is similar to that of synaptic junctions btw neurons → 

Conduction velocity of the action potential, its determinants

Each axon in PNS is surrounded by a sheath of Schwann cells.
Axons can be:
- Unmyelinated = one single schwann cell common for many axons (ca 30 st).
- Myelinated = schwann cell + myelin sheath around one axon.

Development of myelin sheath:
The mesoaxon of schwann cell rotates around axon. The thickness of myelin sheath depends on how many rotations.



The function of myelin sheath = insulate the axon so the impulse can jump from one node to the next – saltatory transmission = 120 m/s.
Myelinated conduct impulses 100 x faster than unmyelinated.

Oligodendrocytes = form myelin sheaths around axons in CNS

Electrical and chemical transmission at synapses

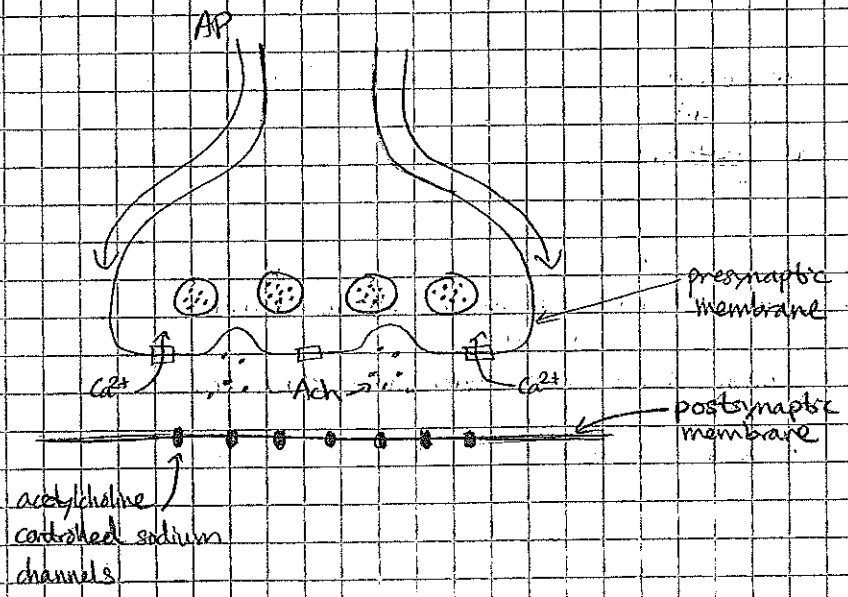
The transfer of AP btw neuron or neuron + target cell is done by means of junctions called synapses.

Electrical synapses = are actually gap junctions between cells. The opposing membranes are connected by protein molecules called connexons. They function as ion channels. Gap ca 3 nm. The ion currents flow through the channels and mediate the AP from one cell to the other.

Ex. btw sensory + motor neurons in neural pathways, and in smooth and cardiac muscle cells.

Electrical synapses are bidirectional.

Chemical synapses = one-directional impulse transfer, from presynaptic to postsynaptic membr. The gap btw membr = 20-50 nm.
The signal is transfered btw cells by means of neurotransmitt.
Usually only one type of neurotransmittor is present in an end bottoun.



The AP causes Ca^{2+} channels to open. Ca^{2+} go into cell & trigger fusion of vesicles containing neurotransmittors (acetylcholine in this case) with presyn. membr.

Neurotransmitt go into synaptic cleft & attach on receptors on postsyn. membr. Cause Na^+ channels to open & Na^+ go into cell ⟹ trigger contraction or new AP to form in postsyn. cell.

Ion channels in neurons + their distribution

The cell membrane of nerves contain many diff. types of ion channels.
Some of these are voltage-gated, some are ligand gated.
It's the behavior of especially Na^+ and K^+ channels that explains the electrical events in nerves.

Na^+ is actively transported outs of cell & K^+ actively into cell.
Conc. of Na^+ is high outside & K^+ inside is high.

Distribution of ion channels

Na^+ channels are highly concentrated in nodes of Ranvier, and in the initial segment of axon.
Around 500 in initial segment, 2000-12000 in nodes of R. and ca 50 on cell body.

K^+ channels accompany Na^+ channels. They are involved in repolarization.

Receptor, synaptic and action potential - description

Receptor potential = is a depolarization caused by inward flow of current. This will usually trigger an AP.
The intensity of the receptor potential determines the frequency of action potentials travelling to CNS.

Ex. taste bud is a receptor. When stimulated it cause some cations to flow into cell. This will trigger AP.

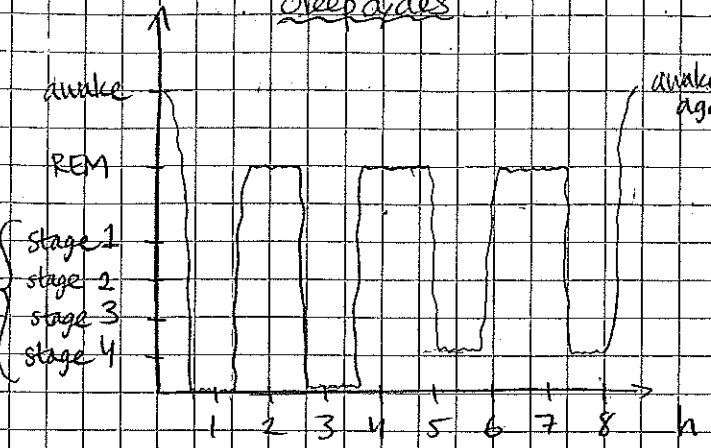
Synaptic potential = also known as postsynaptic potential (PSP). Can be either excitatory PSP or inhibitory PSP. If sufficient amount of EPSP are created an AP is formed.

The synaptic potential is formed when the membrane potential is changed in a neuron due to the input of a synaptic input.

Action potential = You know it!

Things which change membrane receptors:
- Mechanical
- Application to a chemical - NO, Ca^{2+}
- Change in temp
- Electromagnetic radiation

Sleep cycles (nonREM), REM phases



You'll go from awake to stage 4 in 80 min.
Then you gradually alternate btw REM-sleep and non-REM sleep.

The REM-sleep is prolonged all the time. It corresponds to 25% of sleep.

Sleeping is cut into two broad types: rapid eye movement (REM) and non-REM sleep.
Sleep proceeds in cycles of REM and non-REM.

Non-REM sleep has 4 stages they were described by electroencephalography (EEG):

- Stage 1: this stage has waves with low amplitude and high frequency. ~~~~~
  This stage is referred as somnolence or drowsy sleep.
- Stage 2: is characterized by sleep spindles
  Sleep spindles are burst of N-rythm, ranging from 11-16 Hz. ~~~~~
  In this stage conscious awareness of external environment disappears.
  This stage occupy ca 50% of total sleep.
- Stage 3: In this stage slowing + increase of amplitude occurs. ~~~~~
  Body prepares to enter deep sleep. HR slows, temp. ↓.
- Stage 4: characterized by rhythmic slow waves called delta waves. ~~~~~
  This is the deep sleep. If aroused from this sleep feel disoriented.
  This is the stage where parasomnias (sleep disorders) such as
  sleep walking & night terrors occur.
  Night terror = Waking up by gasping or screaming then go back to sleep without remembering waking up

Then you move into REM-sleep. Here most memorable dreaming occurs.
Characteristics of REM are: eyemovements and paralysis of voluntary activity.

Difference btw:

	awake	REM (induced by pons → spikes to occipital lobe)	non-REM
measured by electrooculography (EOG) → Eye movements	moving	moving	no moving
measured by electromyography EMG → Muscle tonus	big tonus	no tonus → paralysis of voluntary activity	smaller tonus

If damaged locus ceruleus = start to move in REM

REM has duration 5-20 min, and occurs every 90 min. Have 4-6 REMs/night.
Active dreaming + active body movements, but muscles are paralysed at this time.

REM-sleep is triggered by pons. Ponto-geniculo-occipital spikes (PGO-spikes) start in pons, they are caused by cholinergic neurons. The spikes project through corp.gen.lat and into occipital lobe and directly after that REM-sleep is triggered.

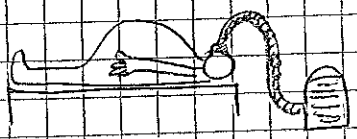
The paralysis of muscles in REM sleep is necessary to protects organism from self-damage through physically acting out scenes from vivid dreams.

If locus ceruleus is damaged, this paralysis disappears and you start to move during REM.

Serotonin = suppress sleep = antisleep.
Adenosin = sleep producing
Coffein = adenosin receptor antagonist.

Sleep apnea syndrom = seen in obese people. Muscles are not able to support open airways because of the fat. During sleep can't breath. Because of $\downarrow VO_2 \Rightarrow$ BP will ↑ and wake up. So several times in deep cycle BP ↑ and you wake.

Treatment is to use CPAP = continuous positive airways pressure.
Patient must sleep with mask which makes pos. pressure.

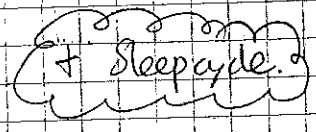


Other sleep disorders:
- Insomnia – not able to fall asleep.
- Somnambulism = sleep walking

Sleep-waking periodicity

Sleep time is controlled by the circadian clock (an inner time, temp. and enzyme controlling device). The circadian clock works together with adenosine. Adenosine is created during day and inhibit sleep. Sleepiness is induced when the circadian elements cause the release of melatonin and when make the body temp. to go down.

It's the circadian rythm that decide how long your individual sleep time is.



EEG, event related potentials

Electroencephalography (EEG) measures and records the electric activity of brain. The signal recorded is called an electroencephalogram.

The electrodes are small disks of silver chloride. They're attached to the scalp above the part of brain you want to examine.

The right side signals are often compared with the left side signals because asymmetrical activity is often an indication of brain disease.

The amplitude of EEG signals are very low : 5-100 μV.
We can distinguish 4 types of EEG waves:

α-waves : f = 8-13 Hz : wakeful, healthy, relaxed adults with eyes closed.

β-waves : f = 18-30 Hz : wakeful, healthy adults with eyes opened.

(γ-waves : f = 30-80 Hz)

theta waves : f = 4-7 Hz : pathological, only physiological during shallow sleep.

delta waves : f = 4 Hz : pathological, only physiological during non-REM sleep. (deep deep)

EEG is used for diagnosis of epilepsy, brain tumours and other brain diseases.
It's also used to investigate sleep-related disorders.

Besides recording electrical activity of brain, it's also possible to measure signals that result when brain receives external stimuli such as flashing lights or sound pulses.
EEG signals of this type are called evoked potentials.

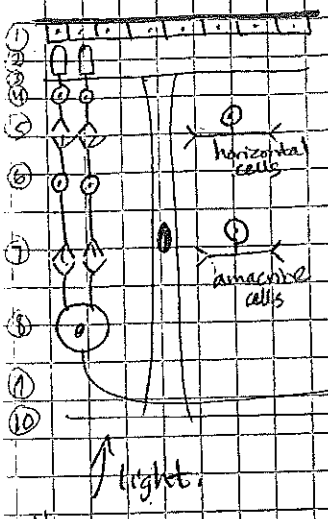
When a normal subject lies quietly with eyes closed an α-rythm is seen. If open eyes it dissappears. If this rhythm is slow or absent it can be a neurological problem.

State of alertness are characterized by waves of lower amplitude and higher frequency.
If presence of epileptiform spikes = sharp waves followed by slow waves it's a sign of abnormality.

Waves of 4-7 Hz recorded over temporal lobes or within hippocampus are called theta rythm, they reflect dysfunction of hippocampal tissue.

Delta rythm are very slow waves. They occur under conditions of severe trauma to the brain (ex. brain tumours). They also occur normally for short periods during sleep.

Description of the connection pattern among the retinal neurons



① Pigment epithelium
② Layer of rods & cones — 1st neuron — - peripheral part of rods/cones.
③ External limiting membrane — - outer bases of Müller cells.
④ External nuclear layer — - nuclei of rods/cones
⑤ External plexiform layer — synapses
⑥ Internal nuclear layer — 2nd neuron — bipolar
⑦ Internal plexiform layer — synapses
⑧ ganglion cell layer — 3rd neuron — ganglionic
⑨ Nerve fiber layer
⑩ Internal limiting membrane — inner bases of Müller cells

Human retina is inverse ⇒ light must pass through most layers of retina before hitting rods + cones

Horizontal cells = establish contact btw photoreceptors, ganglion cells.
Amacrine cells = — " — — " —

Supporting cells = Müller cells = modified glial cells.

Retina:

Vertical connection	Horizontal connection
photoreceptors, bipolar cells ganglionic cells	horizontal cells amacrine cells

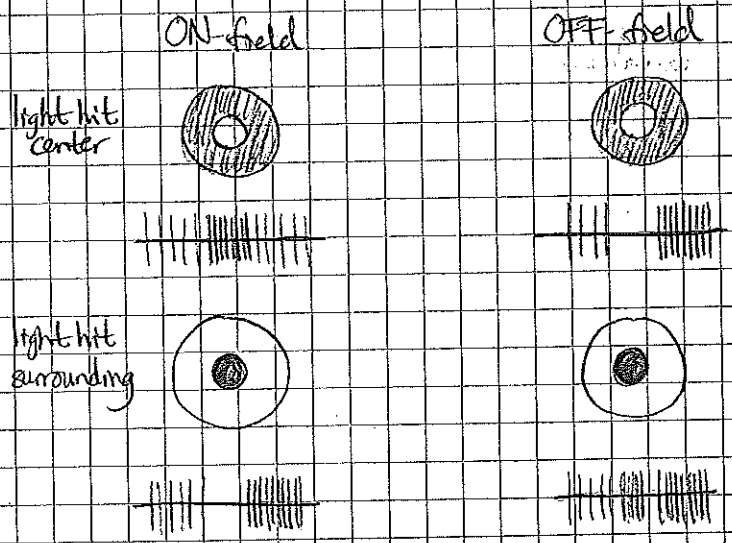
Information processing in retina / Receptive field of retinal ganglion neurons

AP can only be generated in ganglion cells, but local responses and amplitude changes of potentials occur in the other retinal neurons.

In a way, the processing of visual information in retina involves the formation of 3 images. First image is formed by action of light on photoreceptors, it's changed into a second image in bipolar cells and into a third image in ganglion cells. The formation of second image is altered by horizontal cells and formation of third image is altered by amacrine cells.
The third image is the one that reaches the visual cortex.

Bipolar and ganglion cells respond best to a small circular stimulus, called the receptive field. The field has a central zone and a peripheral zone.

The center can be excitatory, with an inhibitory surrounding. = ON-cell, or center can be inhibitory, with an excitatory surrounding. = OFF-cell.



Photostimulation of the center increases the AP frequency of ON-cells.
Stimulation of the perpher, on the other hand, leads to a decrease in AP frequency.

The receptive field of OFF-cells are reverse. If stimulate center, AP frequency ↓, if stimulate periphery, AP frequency ↑

Each photoreceptor cell synapse on one ON-bipolar cell and one OFF-bipolar cell. Each ON-bipolar cell synapse on an ON-ganglion cell and each OFF-bipolar on an OFF-ganglion cell.
A photostimulation of an ON-bipolar cell leads to activation of an ON-ganglion cell ○ stimulation of OFF-bipolar leads to inhibition of their OFF-gangl. cell.

Horizontal cells connect the impulses from periphery of receptor field to the center of the receptor field in bipolar cells.

Monocular o binocular cues of depth analysis

Depth analysis or depth perception is the visual ability to see the world in 3-dimensions. Depth perception arises from a variety of depth cues. Some cues can be processed by one eye some need both eyes.

Binocular cues – These cues provide depth information when viewing a scene with both eyes.
Monocular cues – " " " one eye.

Ex. of monocular cues:

- Motion parallax – when an observer moves, the motion of stationary objects against a background gives a hint about their distance.
  Ex. when driving a car, nearby things pass quickly, while far off objects appear stationary.

- Depth from motion – an object in motion which become smaller appear to move farther away, and objects that appear to be getting larger seem to be coming closer.

- Perspective – when looking at two parallel lines they seem to come close and meet at one point.

- Relative size – ex. two trees are known to be the same size, but one appears larger because it's closer.

- Familiar size – when an object is familiar to us we compare the actual size of it with the perceived size of the object. And thus acquires info about its distance.

- Aerial perspective – objects far away have lower contrast and lower color saturation. So foreground has high contrast and background has low contrast.

- Occlusion – by blocking the sight of objects by others is also a clue which provides info about distance

- Lighting o shading – the way light falls on object and how the shadow is cast provide good info to brain about its shape and distance

- Texture gradient – every surface have a texture, and as the surface goes into the distance, it becomes smoother and finer.

Ex. of binocular cues:

- Stereopsis – in animals which have their eyes placed frontally. By using two images of the same scene, but obtained from slightly diff. angles, it's possible to determine the location of the object. If an object is far away, the difference of the two images falling on retina is small. If object is close the difference will be larger.

- Convergence – in contrast to stereopsis both eyes focus on the same object and by doing so they converge. The convergence is smaller when fix eyes on far object, o big when fix on close objects.

Visual detection of motion

Motion perception is based on visual, vestibular and proprioceptive inputs.

First order motion perception is the perception of motion of an object that differs in contrast to its background, ex. a black bug crawling across a white page.

Second-order motion perception is the perception of motion by looking at the contrast and texture (surface) of the moving objects.

The visual system puts these two motion perceptions together into a 2-dimensional image. And together with binocular and monocular cues a depth perception is created and a 3-D image is created.

Motion has been called the most ancient form of vision. Lions have little use of colour vision because gazelles are the same colour as their surrounding, but lions see motion very well and can see the gazelles running away.
Similar, a frog will instantly snap up a fly passing by, but it won't snap up a dead fly lying on the ground because the frog only respond to motions.

Humans also see moving objects very good.

Conjugate & disconjugate eye movements

M-cells

↓

magnocellular layer

↓

visual cortex

↓

detect movements!

Nondeclarative and declarative memory

Also called explicit and implicit memory.

Memory is an organism's mental ability to store, retain and recall information.
Memory can be divided into:

need to be focused + concentrated

Explicit memory → episodic (for events) - from personal experiences
Explicit memory → semantic (for words) - things we remember from books

Imp. in exams: episodic from practicals, semantic from books

come automatically

Implicit memory → non-associative → habituation, sensitization
Implicit memory → associative → classical conditioning, operant conditioning
Implicit memory → skills - ex skiing, bicycling, swimming. First need to concentrate when learning, but then eventually it works automatically.
Implicit memory → habits
Implicit memory → priming - is facilitation of recognition of words or objects. Ex. if someone say the first few letters in a word, you know the ending of it.

{} Hruška

Explicit memory

To learn anything we need to be consciousness. It's not possible to learn anything while we are asleep. We need to be focused and concentrated.
Explicit memory is the memory which stores facts and knowledge. It's a subject to forgetting, but if frequently assessed it can last indefinitely. Ex. bike riding. First it's an explicit memory when you learn it, but then it becomes an implicit memory when the task is fully learned and it works automatically.

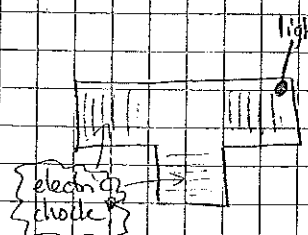
Implicit memory

Does not involve awareness. These memories become unconscious and automatic.

Non-associative form = the organism learn about a single stimulus.
Habituation - if we have a repeated stimuli, the respond will progressively diminish. First time it's applied it evokes a reaction, but eventually the subject becomes habituated to stimulus and ignores it. Ex. if live close to railway, get used to trains.

Sensitization - is the opposite of habituation. A repeated stimulus produces a greater response. Ex. a mother who sleeps with a lot of noise around will wake up immediately when her baby cries.

Associative form = the organism learns about the relation between one stimulus to another.
Classical conditioning - Pavlovs dogs. You give dogs meat and their salivation starts. At same time you ring a bell. After a while it's enough to just ring the bell and the dogs will start salivating.



Operant conditioning - A scientist called Skinner made an experiment with mices. In a box there was some mices. In one corner a light is turned on and at same time an electrical shock was emitted in all other corners except in the light area. The mices will follow the light even though they don't like light because they don't want to get hurt.

Memory can also be divided according to time:

- Working memory – located in prefrontal cortex.
  Ex: if put fork on plate to take the salt, then take the fork again. I remembered where I put the fork.

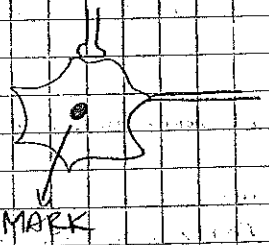
- Short-term memory – located in hippocampus. Lasts seconds to 30 min. It has a capacity to store 3-9 elements. Elements = words, letters.

  In hippocampus there is a circle of neurons which are activated:

- Long-term memory – If the circle is activated several times, finally it becomes long-term memory.
  This memory lasts for years to whole life.

  The process of long-term memory involves a physical change in the structure of neurons in the neural circle.

Cellular mechanisms of habituation and sensitization

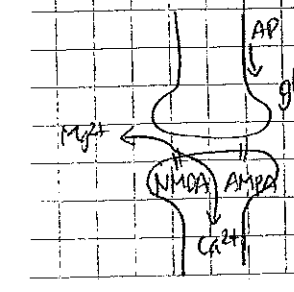


In habituation where the stimulus is repeated over and over, the response to stimuli will gradually disappear. This is done by lowering the release of neurotransmitters from the presynaptic terminal because of low intracellular Ca^{2+}. The low concentration of Ca^{2+} is obtained by inactivate Ca^{2+} channels

2 mechanisms in memory on cellular basis (sensitization)

1) CREB is a protein which is activated by Ca^{2+} which enter the cell when an AP reach the neuron. CREB activate a gene in nucleus called Zif 268 which cause a protein called MARK to be produced. MARK will activate some synapses on the neuron and make them more sensitive. It changes the strength of the synapse.
   MARK = a synapse strengthening protein.

2) AMPA receptor-associated sensitization. AMPA receptors are activated on the post-synaptic membrane. Repeated stimulus of the pre-synaptic neuron cause glutamate to be released in the synaptic cleft. The increased glu will cause AMPA receptors to become activated. Glu binds to AMPA receptor, Na^+ will flow into postsynaptic cell resulting in depolarization. Glu also binds to NMDA receptors but it can't open its channel because its pores are occluded by Mg^{2+} ions. When depolarization occur it will release its Mg^{2+} and channel will be opened. It's permeable to both Na^+ and Ca^{2+}. The Ca^{2+} triggers the upregulation of AMPA receptors ⇒ synapse will become more sensitive!



Specialization of hemispheres

Brain is divided into 2 hemispheres: Right and left. They are linked by corpus callosum. Both hemispheres resemble each other and they have structures which are mirrored by the other side.
Yet, despite that they have similarities, the functions of each hemisphere is different.

Left hemisphere – involved in routine & well rehearsed processing

Right hemisphere – involved in processing novel situations.

The best evidence of hemisphere specialization is language. The major areas involved in language (Broca's & Wernicke's area) are in left hemisphere.

Scientists have studied split-brain patients (where corpus call. is cut) and people born without corpus callosum to better understand the specialization of hemispheres. One of the findings was that right hemisphere was able to rudimentary language processing, but no lexical or grammatical abilities.

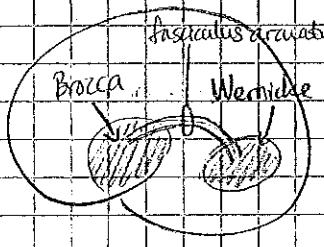
95% of humans have Broca's and Wernicke's area on left hemisphere.
Broca's area – in frontal lobe. Responsible for speech production
Wernicke's area – in temporal lobe. Responsible for understanding spoken language.

The two areas communicate with each other. They're interconnected by fasciculus arcuatus.
Area of Broca lies just in front of motor cortex responsible for tongue movements.

In PET-scan we have studied the diff areas:

Look at words	–	occipital lobe is activated
Speak words	–	broca's area
Listening "	–	Wernicke's area
Think of words	–	many areas activated

So if we hear the language the Wernicke area is activated. If we read the language the cortex in occipital is activated and through connections to Wernicke we can understand the meaning of the words. If we want to speak Broca's is activated ⇒ send info to tongue cortex!



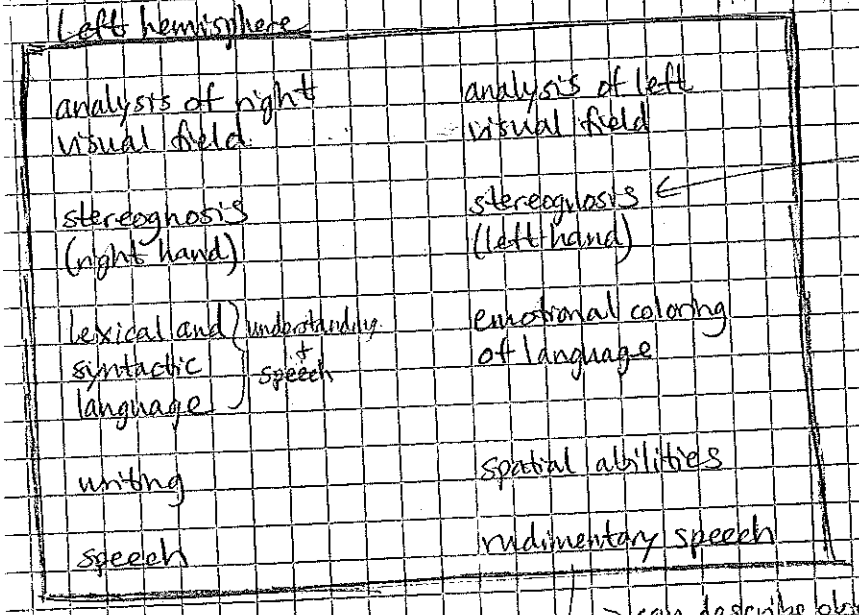
According to modern theory we have 3 systems of language:

- Implamentation system = Broccas, Wernicke, part of insular cortex, BG.
  Serves for analysis of sensory stimuli ex. visual & acoustic stimuli (speak, read)
- Mediating system = connections btw implementary + conseptional systems
- Conseptional system = here all categories & contents are stored.

Speech does not only consist of words, it also consist of gestures.
Right hemisphere has got an analogous area to Wernicke's area which understand the emotional colour of the speech. Ex. if you say "I'm happy" but you look sad. It's called prosody and it's the rythm, stress and intonation of speech. It express the emotional state of the speaker, if the speaker is ironic, sarcastic etc.

If lesion in this area the person can't understand emotional color.

So in conclusion, both hemispheres serves for language, but the "hard work" is done by the left hemisphere, and the "tuning" is done by the right hemisphere.



Dysphonia or aphonia = dysfunction of creation of sound in larynx
Ex. due to cold.

Dysarthria or anarthria = problem with speaking muscles (ex tongue)
Ex. a stroke can influence the motor neurons which innervate the tongue.

Spontaneously active neurons

Many neurons in brain remain active even when animal is at rest. This activity occur even if synaptic transmission to the neuron is blocked! This "spontaneous" firing arises because these neurons have sensitive Na^+ channels which bring the membrane potential to threshold so that an AP can be elicit. Neurons fire impulses spontaneously, without any input.

Two patterns are seen:

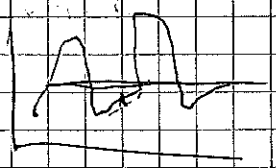
- Regular firing - "beating" - leakage
- Grouped firing - "bursting" -

Regular firing neurons have a less neg. membrane pot. because more Na^+ move into the cell and less K^+ move out. When membrane pot. is moved to a more pos. value the threshold is reached faster, AP is formed.

Bursting neurons: have a slow depolarization. Voltage-gated Ca^{2+} channels are opened, Ca^{2+} move into cell in exchange of Na^+. K^+ channels are activated by Ca^{2+} and open to hyperpolarize the membrane.

↳ depol. is created, but in comparison to Na^+, the Ca^{2+} makes a slower depol.

Spontaneous active neurons are imp. for circuits controlling respiration, locomotion and other activities.



Control of feeding behavior

Is regulated by hypothalamus.
Stimulation of lat. hypothalamus induce feeding behavior = hunger center.
— " — med. hypothalamus suppress feeding behavior. = satiety center.

Lesion in lat. hypoth. is connected with aphagia = inability to swallow
— " — med. hypoth. — " — hyperphagia = excessive hunger

Sensory info via olfaction and taste also play important role in feeding behavior
These signals are sent to amygdala which then convey the signals to lat. hypothala. which intensify the drive for food.

Leptin = a hormone released by adipocytes. In obese people hypothalamus becomes less sensitive to leptin = can't feel when full!

good smell → limbic system + amygdala → lat. hyp. → induce hunger!

Control of fluid intake

Is regulated by hypothalamus by 2 mechanisms:
- By creating the sensation of thirst which makes one want to drink water.
- By controlling the excretion of water in urine.

In lat. hypothal. is a thirst center located. When electrolyte level inside the neurons here become too concentrated the thirst mechanism is activated ⇒ go and drink water.

The control of excretion of water in urine is done by ncl. supraopticus. When fluids in body become too concentrated the neurons here are stimulated and ADH is produced and released in post. lobe of hypophy.
ADH cause reabsorption of water from distal tubule of kidney.

Factors which cause these mechanisms to become activated:
reduced fluid intake, ↑ amount of salt intake, fluid loss due to sweating/diarrhoea, etc...

Temperature regulation = physiological o behavioral components

Body temp. remains constant 36,6 ± 0,6 °C. It is maintained due to some mechanisms:

1) A group of thermo-receptors situated in preoptic area ant. hypothalamus are sensitive to changes in blood temp. If temp. ↑ they stimulate vasodil. and sweating. Leading to heat loss. If temp. ↓ they stimulate shivering which ↑ metabolic rate and thus produce heat.
2) In skin we also have thermoreceptors for warmth and cold. These skin thermo-receptors provide hypothalamic thermoregulatory center with information about the surrounding temperature.
   We use this info ex. when we move from sun to shadow because we sense the sun is too hot.

Core temp is ≈ 37°C, extremities + skin temp varies with environmental temp.
Body must balance the heat loss with the heat absorbed, this is thermoregulation.

Body produce heat during energy metabolism. At rest ca 60% of heat production occurs in inner organs o 20% in muscles o skin.
During physical activity heat production ↑ and the heat production in muscles may rise to 90%.

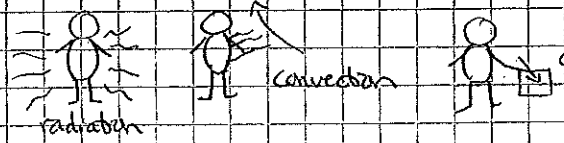
To keep warm, body may generate involuntary muscle contraction called shivering.
Newborns also have so called brown fat which enables to produce heat without shivering.

Heat produced by body is absorbed by blood stream o conveyed to body surface.
Heat loss occurs by:

Radiation = heat from body surface radiates to objects or air which is colder than skin.

Conduction = heat go from warmer to cold by touching an object.

Convection = warm air circulates to a region with cold air
Ex when wind touches skin.



Evaporation — by sweating. About 2500 kJ heat is lost for each liter of H_2O evaporating thus cooling the skin.

Control center for body temp is located in hypothalamus. Other thermosensors are located in spinal cord + skin.
When core temp. rises (eg. during exercise) blood vessels in skin are dilated.
Sweat secretion also ↑. Sweat cools the skin.
When core temp falls: blood vessels constrict o ↑ heat production by generating involuntary muscle contraction (shivering).

Sexual differentiation of brain

- sexual differentiation of brain is dependent on hormones.

Sex hormone levels in male and female fetuses and infants differ. In brain both androgen and estrogen receptors have been found. The difference of exposure of these hormones to brain produce differences of brain structure and function in females and males.

Structural differences begin to show by 2 years of age which include size o shape of corpus callosum and certain hypothalamic nuclei

All types of sex hormones are present in both ♀ o ♂, but their balance is diff.
Testosterone predominate in male
Estrogen o progesteron in females.

These sex hormones act on neurons in brain through receptors. They can either activate or inhibit specific gene expression.

Some differences, ex: nr. of neurons in corpus callosum is greater in ♀ than ♂.
thickness of left side cortex is bigger than right in males.

Sex differences is also seen in cognitive performance. Ex. men are better to orientate themself in their surroundings than women, but women are better in verbal tasks, the ability to solve problems using language.
Women are more likely than men to recover speech after a stroke that damaged cortical speech areas.

Apparently estrogen is the hormone which masculinizes the brain.
The question is why estrogen don't masculinize the female brain?
Apparently females have a protein called α-fetoprotein present in blood. It binds to estrogen and prevent it from entering the neurons in fetal brain.

Males however lack this α-fetoprotein. Testosterone is not bound to it, and can thus enter the neurons. In neurons testosterone is converted to estrogen and it exerts its masculinizing action!

How does it work in homosexual humans?

3 structural differences have been observed in brains of homosexual:

- Suprachiasmatic nucleus — larger in homosexual men than heterosexual men
- Hypothalamic nucleus INAH-3 — smaller in homosexual men, same size as female.
- Anterior commissura — larger in homosexual men.

Also genetic factors may play a role. Ex. occurence of homosexuality in both twins is much higher, than only in one of them.

Peripheral component of parasympathetic compartment of ANS, neuron cell distribution

Divided into:

Pars cranialis ⟶ In brainstem as:
- Nd. Edinger-Westphal
- Nd. salivatorius sup + inf.
- Nd. o. dorsalis n. X

Pars sacralis ⟶ 3rd-4th sacral root.

Pars cranialis

Nd. E.W fibers via n. III to ggl. ciliare ⟶ m. ciliare, m. sphincter pupillae.

Nd. salva. sup. ⟶ n. VII ⟶ n. petrosus maj. ⟶ ggl. pterygopal. ⟶ gll. lacrimalis

Nd. salva. inf. ⟶ n. IX ⟶ n. petrosus min. ⟶ ggl. oticum ⟶ gll. parotis

Nd. salva. sup. ⟶ n. VII ⟶ chorda tympani ⟶ ggl. submand. ⟶ gll. submand.

Nd. o. dors. n. X ⟶ n. X ⟶ intramural ganglia in organs. ⇒ innervate heart, lungs, stomach, liver, pancreas, kidneys, intestine.

Pars sacralis

From S2-S4 fibers go to ganglia in plexus hypogastricus inf. ⇒ innervate rectum, urinary bladder & genitals.

Peripheral component of sympathetic compartment of ANS, neuron cell distribution

Symp. nervous system. In cornu lat., C8-L2.
Neurons here send communicating branches to truncus sympathicus, divided into:
- Cervical segments - ganglion cervicale sup, medium and stellate.
- Thoracic segments - 10 ganglia
- Lumbar segments - 4 ganglia
- Sacral segments - 4 ganglia
- Coccygal segment - ganglion impar

ggl. cerv. sup - its postgangl. fibers form plexuses around a. carotis int. + ext. which reach eyes ⟶ m. dilator pupillae + glands of head.

All cervical + upper thoracal ganglia send postgangl. to form plexuses around heart + lungs together with parasymp. fibers from n. X.

Branches from thoracal + lumbar ganglia send postgangl. to prevertebral ganglia: ggl. coeliaca, ggl. mes. sup., ggl. mes. inf. which supply organs such as pancreas, spleen, stomach, liver, intestines, rectum.

Symp. NS - work during day. Activated by stress.
↑: BP, HR, dilate pupils, raise hair
↓: peristaltic activity + secretion of intestinal glands.

Parasymp. NS: - work during night. Activated by "rest & digest".

Structure of enteric nervous system

Enteric NS consists of neurons in the wall of the gut. They regulate gastrointestinal motility and secretion.
It consist of 2 layers of neurons, present in the smooth muscle layer of gut:

1) The myenteric (Auerbach's plexus) → control gastrointestinal motility
2) The submucosal (Meissner's plexus) → control water & ion movement across the intestinal epithelium.

The enteric NS is controlled by symp/parasymp. NS.

The sympathetic innervation is derived from branches of thoracic, lumbar and sacral sympathetic trunk. These fibers are postganglionic.

The parasympathetic innervation is derived from vagus and pelvic nerves.
These fibers are preganglionic

Chemical transmission at autonomic junctions

Parasymp. NS: pre- and postganglionic fibers transmit impulses by acetylcholine.

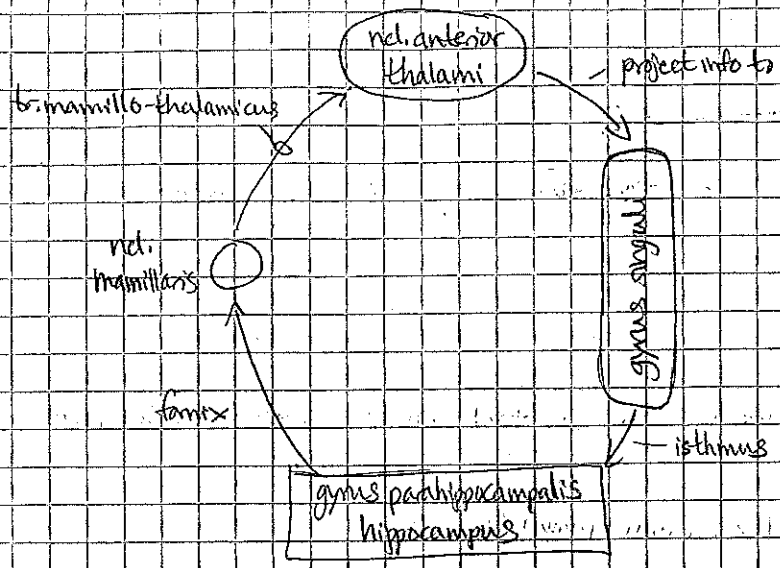
Symp. NS: preangl. fibers transmit by acetylcholine
postangl. fibers transmit by noradrenaline (except postgangl. symp. of sweat glands of skin = also acetylcholine).

Cholinergic receptors - There are two types: muscarinic and nicotinic receptors.
Muscarinic are located in myocardium, smooth muscle cells and in exocrine glands.
Stimulation of these receptors cause ↓ in heart rate, miosis, secretion of different glands (lacrimal, salivary, sweat glands & GIT glands).
Nicotinic receptors are located in adrenal medulla and in autonomic ganglia.
If stimulated in adrenal medulla they cause release of epinephrine and norepinephrine from cells in medulla.
Acetylcholine is the transmitter which bind to cholinergic receptors.

Adrenergic receptors - activated by noradrenaline. Divided into 2 major classes:
α and β adrenergic receptors.
α_1 - stimulation cause vasoconstriction, bronchoconstriction & motility of GIT is inhibited.
α_2 - stimulation cause glandular secretion inhibition
β_1 - located in heart, stimulation cause ↑HR & contractility
β_2 - located in smooth muscles (ex. bronchial smooth muscle), stimulation cause relaxation of these muscles, ex. bronchodilation.
β_3 - located in adipose tissue, stimulation lead to mobilization of fat stores = thermogenesis!

Cerebral system of emotion and stress – major structures & pathways

James Papez described 4 principal structures connected in a circuit which he suggested to form the anatomical site for emotion.



However, we don't know the specific function of this circle, plus that other structures are also involved in emotional behavior, so we now use the term Limbic forebrain

See:
Also amygdalar nuclei
+ neural circuit of fear

Limbic system play role in olfaction, sexual behavior, emotion of rage, fear and motivation.
Emotions can't be turned on/off at will ⇒ due to prolonged after discharge!

Olfaction – olfaction & sexual behavior are connected. There are substances called phemones which are sexual attractants in animals.

Sexual behavior – urge to mate.

Fear – avoidance reaction → fleeing
Rage – attack reaction → fighting

Structures responsible for this:
Amygdala nuclei + ventromedial nuclei in hypothalamus
If destruction in amygdala = placidity
— " — VMN = rage

Motivation – self-stimulation. Reward-system = nucleus accumbens
Ex. when we eat some tasty food ventral tegtal area is activated and it activates ncl. accumbens.

VTA —dopamin→ NA

We have 3 types of drugs which modify behavior:

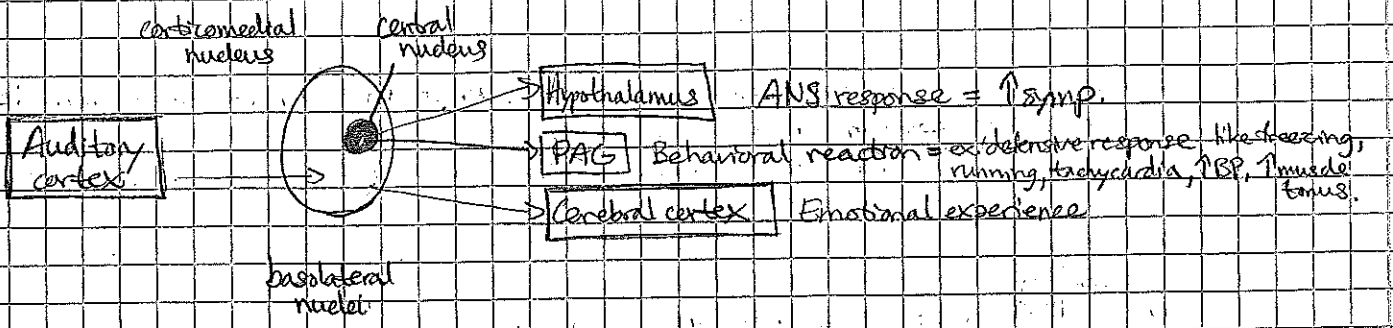
- Hallucinogenic
- Tranquilizers
- Anti-depressant

+ Ex. LSD
+ eliminate anxiety. Drugs activate GABA receptors which ↑ Cl^- conductivity which makes anxiety disappear!

↳ ☹ → ☺ Ex. Prozac. It activate release of serotonin ⇒ our mood ↑.

Components of a defensive response

Neural circuits for learned fear:



Learned fear = based on the voice. Ex. if hear sound of a wire at the dentist you can imagine the pain in tooth made by this instrument.

Auditory cortex send to basolateral ndll. (amygdala)
Signal is elaborated in amygdala and through central nucleus signals are sent to hypothalamus & PAG.

Cerebral cortex in frontal lobe is related to our experience. We know that this sound is connected with pain. Amygdala sends signals to this cortex and activate it.

Fear & rage (fleeing or fighting) are part of limbic system.
Structures responsible for this: amygdalar nuclei & ventromedial nuclei in hypothal.

Ventromedial nucleus (VMN) is associated with satiety.

PAG = also involved in analgesia

limbic syst + amygdala
↓
PAG
↓
RF brainstem = ndl. raphe
↓
spinal motor neurons

PAG stimulate ndl. raphe which secrete serotonin. Serotonin activate some interneurons in spinal cord which release enkephalin. Enkephalin binds to opioid receptors on the incoming axons which carry pain info. (C- and Aδ-fibers). This make their pain signals to become supressed.

Control of sexual behavior

Mating is regulated to a large degree in the limbic system and hypothalamus. The basic responses are innate and undoubtedly present in all mammals, because mating can occur with no previous sexual experience.

Sexual behavior is dependent on endocrine function. Removal of gonads lead to ↓ sexual activity, in both ♀ & ♂.
Testosterone in males and estrogen in females have the most marked effect.
Both testosterone and estrogen ↑ libido (= sexual interest).

♀ sex behavior:
One of the key structures controlling sexual behavior is ventromedial hypothalamus (VMH). It contains estrogen & progesterone receptors. Stimulation of this area induces a sexual response called lordosis. It's characterized by the female arching of the back and a deflection of the tale which allows intromission of the male.

Hypothalamus also involve the release of GnRH from ant. hypothalamus (preoptic region). GnRH stimulate FSH secretion which in turn ↑ estrogen levels

♂ sex behavior:
Is induced by the presence of testosterone. Testosterone acts on the preoptic region which produce a sexual behavior.

Phermones = substances produced by an animal that act at a distance to produce hormonal, behavioral or other physiological changes in another animal of same species. Ex. sex attractants of certain insects.

In humans phermones also have an effect. Ex. women who are good friends or roommates tend to synchronize their menstrual cycles.
Also, infants prefer pads wiped on breast or axillary areas of their own mothers over pads from unfamiliar women.

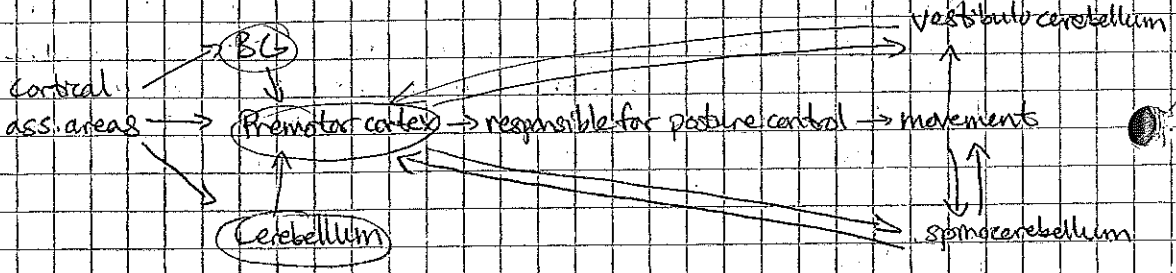
Control of locomotion

There are 2 types of movements:

- Reflexive
- Voluntary

Reflexive = signal from outside don't reach the brain, it enters spinal cord and response is sent back directly from cord to muscle.
Ex. if put hand on a warm plate, will take it away immediately.

Voluntary = You get an idea of moving an object (ex. a pen)
Cortical associations areas will be activated and send signals to 3 structures:



Signals are sent to BG, premotor cortex & cerebellum. BG & cerebellum will influence the premotor cortex.
Signals will be sent futher to motor cortex which will send info to muscles to perform the movements.

Movements in muscles will send info to vestibulocerebellum and spinocerebellum.
Spinocerebellum control the smooth movements
Vestibulocerebellum is responsible for posture control.

Signals from motorcortex will travel through capsula interna.
80% of fibers will cross midline in pyramid & form tr. corticospinalis lat. = responsible for fine skilled movements, fine movements of fingers etc..
20% of fibers will not cross midline, they will form tr. corticospinalis ant. = responsible for gross movements, axial movements ex. bending back etc.

See also: Medial system – cortical pathways
Lateral system – " "

Postural control

To maintain body in an upright, balanced position it needs some postural control, or adjustments.
Postural control include: - Static reflexes
- Phasic (dynamic) reflexes.

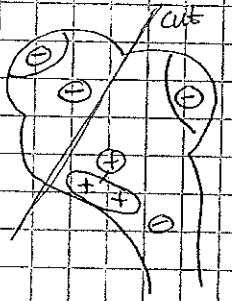
Phasic reflexes involve transient movements, short-term movements.
Static reflexes involve sustained contraction of muscles.

Posture is controlled by motor centers in brainstem, ex. the red nucleus, vestibular nuclei and RF.
↳ se (g. hierarchic org. of M-s system + g. medial/lateral systems/brainstem pathways)
Input is received from labyrinth organs & proprioceptors in muscles.
Also input from skin receptors, eyes, ears also play a role in posture control.

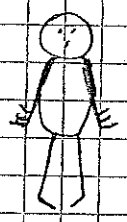
Descending tracts to spinal cord from nel.ruber + RF in medulla obl. (tr. rubrospinalis + tr. reticulospinalis lat.) have an inhibitory effect on α & γ motorneurons of extensor muscles and excitatory effect on flexor muscles.

On the other hand, Deiter's nucleus + RF in pons inhibit flexors & excite α + γ of extensors.
(to flexor/extensor muscles)

Normally there is an equal distribution of inhib./stim. neurons, but if we make a cut, it will not be equal any more. Ex. a transection of brainstem below nel.ruber will lead to decerebrate rigidity because the extensor effect of Deiter's nucleus predominates.



Decerebrate rigidity, develops as soon as brainstem is transected. Patient will form a posture like this, and then die.



Decortical rigidity - develops when transection is made above nel.ruber. This will lead to patient lying in a position like this:

If the head of a decerebrate patient is turned to the side, the limb on one side becomes extended & the limb on the other side becomes flexed. This response is called the tonic neck reflex. It's initiated by stretch of the proprioceptors in the upper part of neck.

Spinal cord damage

Transection of spinal cord is followed by a period called spinal shock during which all spinal reflex responses are depressed. After a while, ex. 14 days, the reflex responses return to normal.

Patients with chronic spinal damage can use noxious stimuli at the part of body where the paralysis is to stimulate autonomic centers and produce evacuation of bladder and rectum. They initiate micturition/defecation by pinching their thighs producing an intestinal mass reflex.

Paralysis = complete loss of movement = damage of fibers from α-motor neurons to effector.

Paresis = If some upper neurons are damaged we can still have some movements. Divided into:

- flaccid paresis = the force of movements is ↓.
- spastic paresis = in children which were damaged during fetal life.
- incoordination paresis = caused by damaged cerebellum, the movements will be big.

Effects of cerebellar lesions on motor functions

Humans with lesions of cerebellar hemispheres show no abnormalities as long as they are at rest. But when they move abnormalities are shown.

All movements are characterized by a marked ataxia.

Ataxia = errors in the rate, range, force and direction of movement.

If cortex of cerebellum is damaged = compensation occurs and the movement abnormalities gradually disappear.

If cerebellar nuclei are damaged = the abnormalities are permanents.

Symptoms:

Speech become slurred

(1) Voluntary movements are abnormal. Ex. attempting to touch an object with fingers results in overshooting to one side. This is called dysmetria. It initiates a gross corrective action, but the correction overshoots to the other side. Consequently the fingers oscillates back and forth, this is called intention tremor

The tremor is absent at rest, but it appears as soon as the patient attempts to perform some voluntary movement.

(2) Another characteristic of cerebellar disease is inability to "put on the breaks" for example stop movement promptly.
Ex. if cerebellar lesion a patient can't stop the movement of the forearm if flexion against a resistance suddenly disappears. The arm will fly backwards in a wide arc. This abnormal response is called the rebound phenomenon.

(3) Finally, patients with cerebellar disease have difficulty performing actions that involve many joints at same time. Instead they carry them out one joint at a time, a phenomenon called decomposition of movements.

The person becomes slow to orient its extremities in space. He's got an inability to judge distance & can't receive and process information rapidly. He can't respond in a fine-tuned response.

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Disease of the basal ganglia in humans – motor consequences

Diseases affecting BG produce marked & characteristic abnormalities of motor functions.
Diseases of BG are of 2 types:

- **Hyperkinetic abnormalities** = in which movements are excessive and abnormal
  This include:
  - Chorea = involuntary "dancing" movements
  - Athetosis = slow writhing movements
  - These two types of movements are often seen at the beginning of the voluntary movement, they happen involuntary.

  Also include ballism = involuntary flailing, intense and violent movements occur.

- **Hypokinetic abnormalities** = include akinesia & bradykinesia
  Akinesia = difficulty in initiating movements
  Bradykinesia = slowness of movements.

Huntington's disease

In BG normally 3 pathways operate in a balanced fashion:
1) Nigrostriatal dopaminergic system.
2) The intrastriatal cholinergic system
3) The GABAergic system which projects from striatum to globus pallidus & subst. nigra.

In Huntingtons, a loss of GABAergic & cholinergic neurons occurs in BG.
The loss of GABAergic pathway to external pallidum releases inhibition, permitting hyperkinetic features to develop.

Parkinson's disease

Degeneration of nigrostriatal dopaminergic system.
The fibers to putamen are most affected.
Symptoms appears when 60-80% of the nigrostriatal dopaminergic neurons are lost.

Parkinson has both hypokinetic & hyperkinetic features.

The hypokinetic features = akinesia & bradykinesia.
The hyperkinetic features = rigidity & tremor.

Has difficulty to initiate voluntary movements and there is a decrease in associated movements, ex. unconscious movements such as swinging arms during walking.

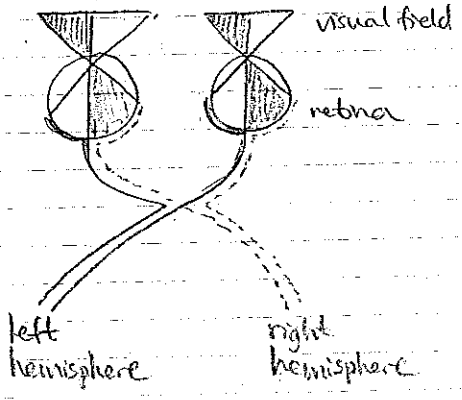
Pathways that convey visual information to cortex, their functional significance + projection of visual info to tectum a hypoth., description a functional significance

Visual pathway:

I neuron – rods + cones
II " – bipolar cells
III " – ganglion cells
IV " – ncl. corporis geniculati lateralis
V " – primary visual cortex

Ca 10% of signals will however travel by radix medialis tr. optici to:

- **Tectum (mesencephalon)** – tr. retinotectalis
  - → nd. colliculi sup. → reflexes for pursuit a saccadic eye movements
  - → pretectal area → control of accommodation a pupillary reflexes. ⇒ see q pathways for miotic/mydriatic pupillary reflex!
- **Hypothalamus** – tr. retinohypothalamicus
  - → suprachiasmatic ncl. → control of circadian rythms eg. Heliotropic stimulatory system because its linked to the release of melatonin
- **Pulvinar thalami**
  - Coordination of visual a somatosensory perception



Visual cortex, its division and individual contribution to analysis of the visual information

Axons of gangl. cells project into lateral geniculate body. Each body contain 6 layers.
Layer 3-6 have small cells and ace called parvocellular
Layer 1-3 have big cells = magnocellular.

Layer 1, 4 o 6 receive input from the contralateral eye.
The rest recieve info from the ipsilateral eye.

Only 10-20% of info to lat.gen.body comes from retina. Major inputs comes from visual cortex o other brain regions. These signals from brain are imp. in the perception of orientation o motion.

Two kinds of gangl. cells can be distinguished in retina;
Large gangl. cells (magno, or M-cells) = are concerned with movement o stereopsis.
Small gangl. cells (parvo, or P-cells) = concerned with color, texture o shape.

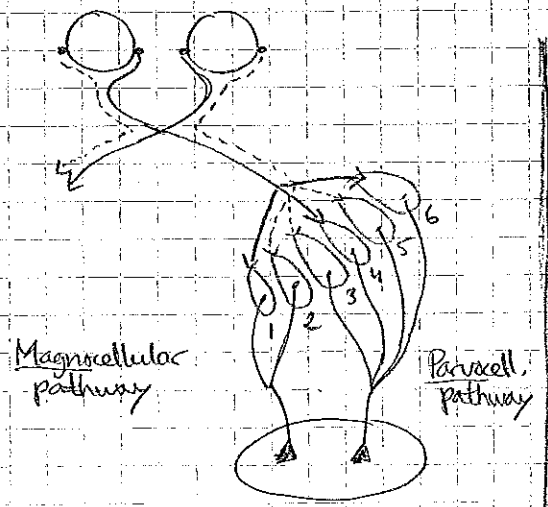
M-cells project to the magnocellular portion in body.
P-cells to parvocellular portion.

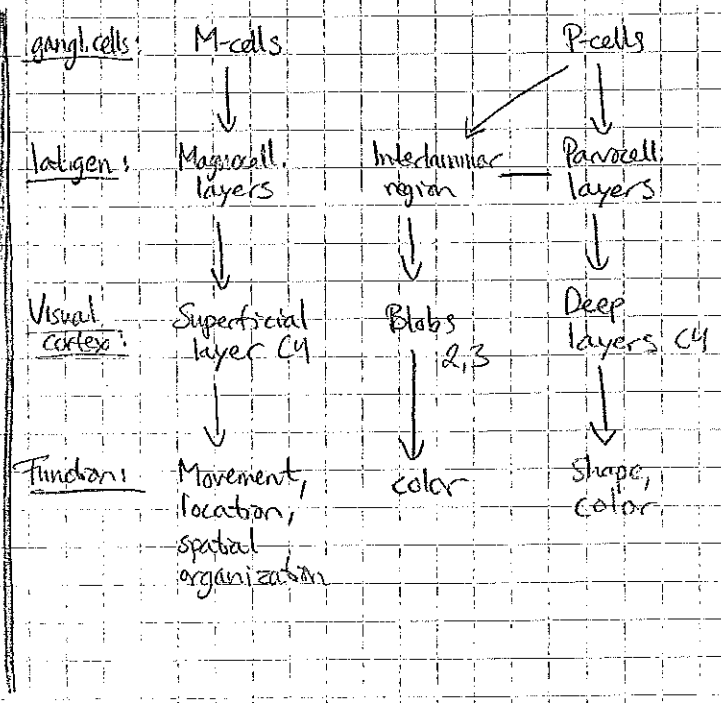
From the lat.gen.body a magnocellular pathway and a parvocellular pathway project to visual cortex.

Magnocellular pathway (from layers 1+2) carries signals for detection of movements, depth and flicker.

Parvocellular pathway (from layers 3-6) - signals for color vision, texture, shape and fine details.

Cells in intralaminar region of lat.gen.body also receives input from P-cells.
They project signals via a separate P-pathway to the "blobs" in visual cortex.
Blobs are sections of visual cortex where neurons are sensitive to color, they assemble in cylindrical shape.





Visual cortex has 6 layers. Axons from magnocell. pathway end in layer 4, in its deepest part 4C. Parvocell. pathway also end in 4C, but more deeply.

Axons from interlaminar region end in layers 2 & 3.
Layer 2 & 3 contain clusters of cells called blobs. Are concerned in color vision.

Glial cells & their role in the ontogenetic development of CNS

Glial cells = supporting cells of CNS, are non-excitable.
Classified into: astrocytes, oligodendrocytes, microglia & ependymal cells.

Astrocytes

Star-shaped. Their processes are often in contact with blood vessels.
Some neurotransmitters (ex. glutamate & GABA) are taken up by astrocytes & processed for recycling.

Two kinds of astrocytes:
- Protoplasmic → prevalent in grey matter.
- Fibrous → prevalent in white matter

Müller cells in retina are a type of modified astrocytes.

Oligodendrocytes

Are found in white matter. They produce the myelin of myelinated axons in CNS.

Microglia

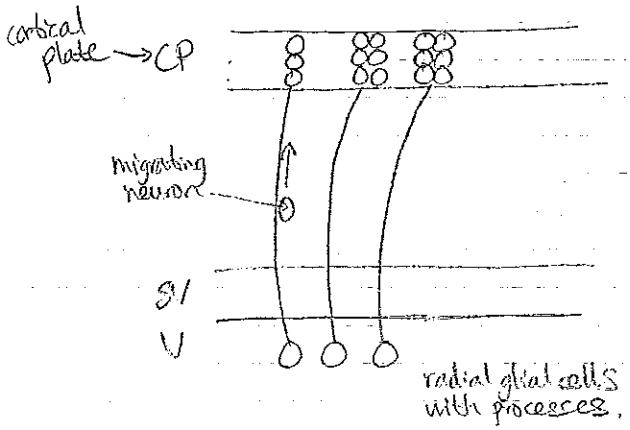
Smallest glial cells. Play a part in defense mechanism. In case of tissue damage, microglia differentiate into phagocytic cells.

Ependymal cells

Line the ventricles of brain. Responsible for the production of CSF.
Ependymal cells + associated capillaries = choroid plexus.

Role in ontogenetic development

In the developing brain radial glial cells help neurons to migrate into their right positions. => se also g. developmental zones →



Glial cells and their role in the ontogenetic development of PNS

Glial cells of PNS include: · satellite cells = within ganglia of PNS
· schwann cells.

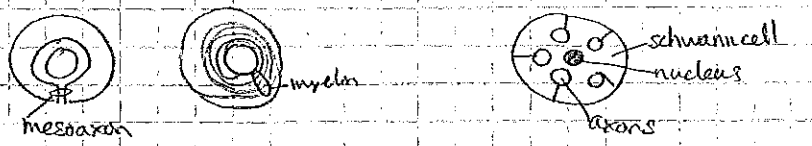
Satellite cells

They surround ganglion cells in one layer. Transport nutrients btw ganglion cells + capillaries.

Schwann's cells

Take part in myelin formation, in PNS. Each axon in PNS is surrounded by a sheath of Schwann cells.

2 types: · Unmyelinated = one single schwann cell + many axons (up to 30 st)
· Myelinated = one schwann cell + myelin sheath + one axon.
The myelin sheath is produced when the mesoaxon of schwann cell rotates around the axon.



(ontogenetic = origin + development)

Role in ontogenetic development

Describe development of neural tube, mention radial glial cells....
Wallerian degeneration!

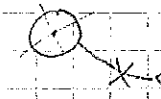
Reactions of the CNS & PNS glial cells following injury (Wallerian degeneration)

After injury to an axon, both intrinsic and extrinsic factors play a role to re-build the axon again.

There is a difference if the neuron is damaged in CNS or in PNS.

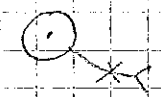
INTRINSIC F.

CNS



In CNS, if damage to axon, the neuron will die.
If damage is made at end of axon only a small amount of cytoplasm is lost, so neuron will survive longer. If damage is made close to soma, neuron will die fast.
It is said that the neurons have a catabolic character. They have no capacity of regeneration.

PNS



In PNS, if damage to axon, neuron will survive, because it exhibit anabolic character. The anabolic processes which act to renew the axon are, ex.

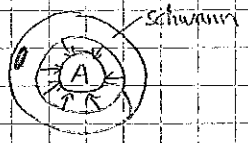
- ↑ synthesis of skeletal & membranous molecules
- Neurofilaments [illegible] in site
- ↑ synthesis of hydrolytic enzymes and ↓ synthesis of enzymes which produce/degrade neurotransmitters,

EXTRINSIC FACTORS

Glial cells acts in:

CNS: ↑ microglial cells ⇒ phagocytic cells
Oligodendrocytes + astrocytes ⇒ has nothing to do with regeneration of axon.

PNS: ↑ satellite cells in ganglia = support neurons.
↑ proliferation of Schwann cells distal to the injury.
The schwann cell will stimulate, send trophic signals to the damaged axon to regenerate axon.



Wallerian degeneration

Before the axon can regrow the old, damaged axon must be degraded in a process called Wallerian degen.
The fragments of the axon + its myelin sheaths are degraded by macrophages from blood and cleaned up, then Schwann cell proliferate.
Some non-differentiated schwann cells will line inside the basal lamina to form columns called Büngner's columns
These columns will up-regulate synthesis of neurotropic and neurotrophic factors, stimulating axonal growth.

There are two sorts of reconnection:

① Reconnection in the same pathway as the old axon to reach the target structure, via Wallerian reconnection. Reach the original target structure. This is the way when ex. only a part of nerve is damage, ex. during carpal tunnel syndrome.

② If nerve is cut completely we may connect the endpieces by sutures or if the cut is too large we may connect them with a nerve graft. The nerve can regrow inside the graft. For nerve gratts we can use cutaneus nerves, eg. n.suralis. It's long & only innervates a small skin area of foot.

Molecular mechanisms for axon navigation to the target tissue during development and regeneration of the nervous system.

In regeneration = plasticity

growth cone – is an imp. terminal component of growing axon. It has fingerlike processes which it uses to examine the surface of the target. It looks for permissive & non-permissive molecules so it know where to grow.

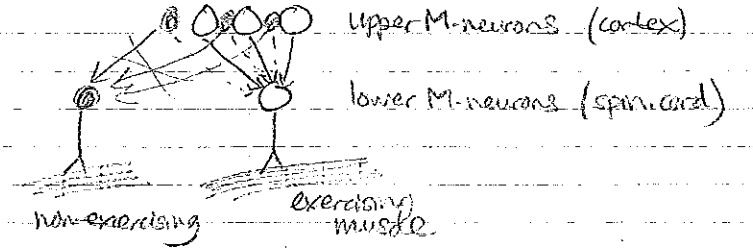
There are 2 types of plasticity:

- Adaptable plasticity = provide structural & functional conditions for adapting the NS to external changes.
- Reparable plasticity = correct errors or small interruptions in NS, during normal activity or after injury = Wallerian degeneration

Rebuilding synapses at adaptable changes of NS

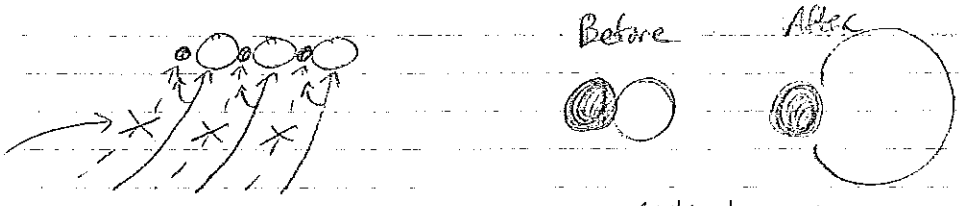
Ex. during ↑ intake of signals (afferentation). Ex. during long term exercise. Muscle which is excersised will produce more neurotrophins. This will support the motor neurons which innervate the muscle.

In cortex there are many motor neurons. Some of them innervate the lower motor-neurons in spinal cord which innervate the exersising muscle. Some other motor neurons in cortex innervate lower motor neurons for another muscle which is not exercised. When this muscle is not used, its motor neurons in cortex will start sending their axons to the exercising muscle's lower motor neurons instead. The non-exercising muscle will undergo atrophy = become weaker.



Experience-dependent plasticity

The cortical map of sensory function will be increased or decreased.
Ex. if loose an arm. Some neurons in cortex will loose their afferentation. Instead some other neurons in cortex (next to them free of aff.) will start to send axons to them. This will result in a cortical differentation.

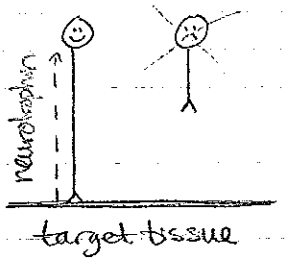


If cut aff. to these neurons they won't recieve any signal.
White will send axon ⟹ makes cortex more specialized in reciving aff. from white neurons.

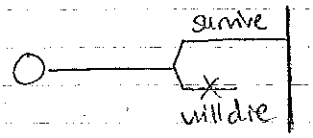
Axon navigation to target tissue during development

During development a lot of neurons are produced. They send axons to tissues. But only those who reach the tissue can recieve neurotrophins & survive. The ones which send off their axons too late (not within the time of the critical period of neurotrophic factors) will die, because their axons won't reach the tissue.

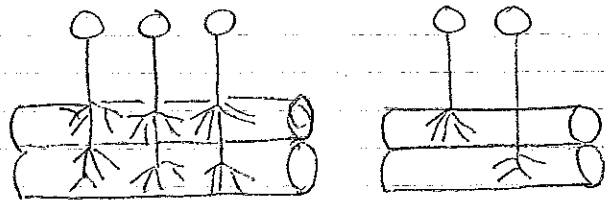
Each tissue produce it own attractive molecules called neurotrophins. These molecules stimulate the growth of the axons. Neurons will only send off axons to tissues which secrete neurotrophins.



The same happens with synapses. If axon sends synapses fast to target tissue they will get enough neurotrophin and they will survive. If send synapses too slow, the synapse will die.

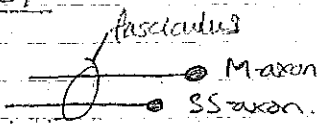


In beginning many terminal synapses will be formed on many muscle fibers, then a reduction of synapses occurs and synapses from a specific neuron will focus on only a few fibers.



How does the motor axons and SS-axons reach their target tissue?

Motor axons will navigate the SS-axons by fasciculization.
M-axons grow first & SS-axon will follow and they will form the peripheral nerve.

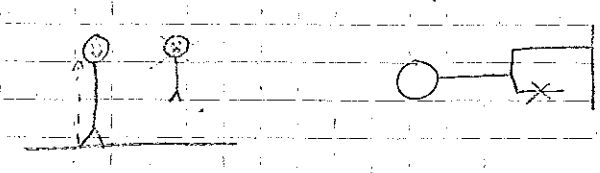


Axon navigation has 4 molecular mechanisms:
1. Fasciculation
2. Attractive molecules = neurotrophins
3. Permissive surface
4. Non-permissive surface

Motor axons will attach to surfaces with high conc. of permissive molecules & not on surfaces with non-permissive molecules.
Ex. in somets. In rostral part are ↑ conc. of permissive mol. ⇒ here motor axons attach. Caudal part has ↓ nr. permissive mol. Rostal will grow faster and this leads to a diff. development of vertebral column & spinal cord.

Trophic interactions among the neurons and target tissue, neurotrophic factors and their characteristic features

Trophic effect (Trophism) = ability of certain molecules called trophic molecules to stimulate cell survival. They stimulate growth & regeneration of cell.



Se föregående sida!

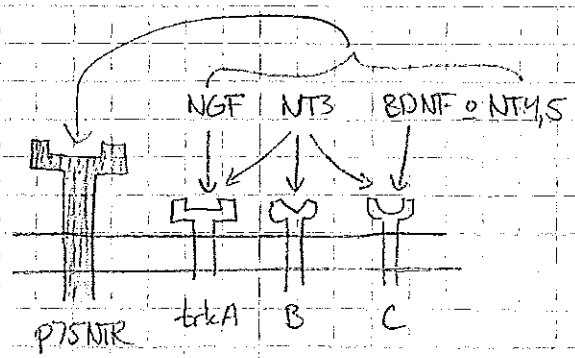
Neurotrophic factors:

- NGF = nerve growth factor
- BDNF = brain derived neurotrophic factor
- NT-3 = neurotrophin 3
- NT4,5 = neurotrophin 4/5.

The neurotrophic factors interact with 2 types of receptors:

- tyrosin kinase receptors: trkA, trkB, trkC
  or
- p75NTR-receptor

All four factors can bind to p75NTR.
NGF binds to trkA
NT3 binds to trkA, B, C
BDNF & NT4,5 binds to trkB.



When molecule binds to trk the trk becomes phosphorylated on its intracellular tyrosin residues, and it also start to phosphorylate intracellular proteins. These proteins become activated and can bind to other proteins and activate a lot of signal pathways!

Selective neuronal death during ontogenetic development of NS, describe a mechanism and its significance.

Se föregående sida + neurotrophins! Kan också prata om Wallerian degeneration!

Developmental zones of neural tube during histogenesis of CNS, cell populations originating from neural crest

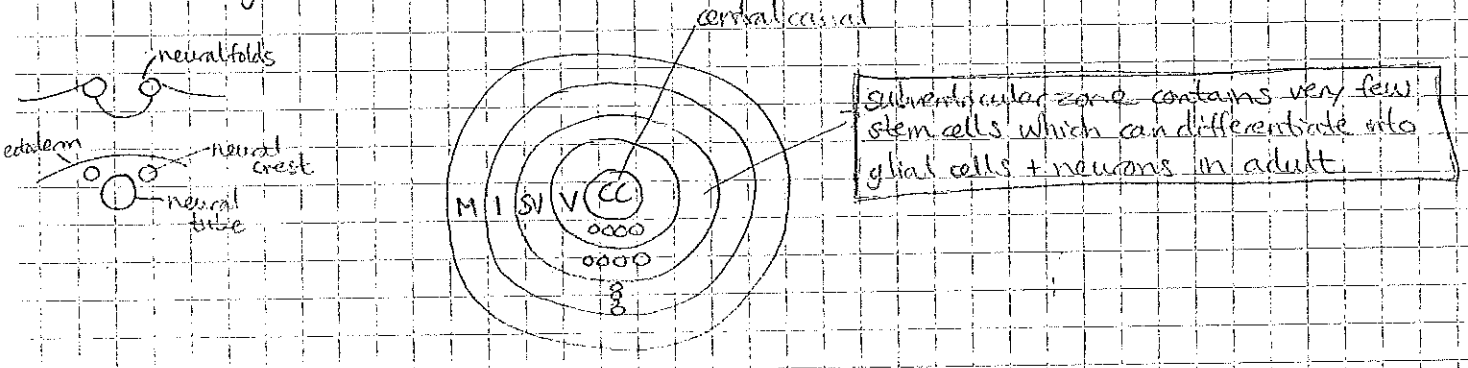
CNS develops from a thickened area of the embryonic ectoderm = neural plate
It occurs on the dorsal aspect of the embryonic disc.
On day 18, neural plate begins to invaginate & forms a neural groove, limited by neural folds on each side.
Neural folds will move together and fuse to a neural tube.
When neural folds fuse, some neuroectodermal cells separate from them and form a single cord called neural crest.
Neural crest cells give rise to cells of spinal ganglia & autonomic ganglia.

The proximal end of neural tube → future brain.
Caudal end → spinal cord.

The wall of neural tube differentiate into some zones:

- ventricular zone
- subventricular zone
- intermediate zone
- marginal zone

} Contain neuroblast (future nervecells) & glioblasts which will migrate to intermediate zone & organize into two collections of cells: the alar plate & basal plate.



In ventricular zone some radial glial cells are present. They will send off long processes to marginal zone. Along the processes neurons will migrate to outer zones and organize into columns.

This is how the cerebral cortex develop, neocortex, which have 6 layers.

Development of spinal cord

Cells in basal plate become efferent (motor) neurons ⇒ will form ventral horn.
" " alar plate " afferent (sensory) neurons ⇒ " " dorsal horn.

Development of brain

First 3 primary brain vesicles forms:

- Forebrain
- Midbrain
- Hindbrain

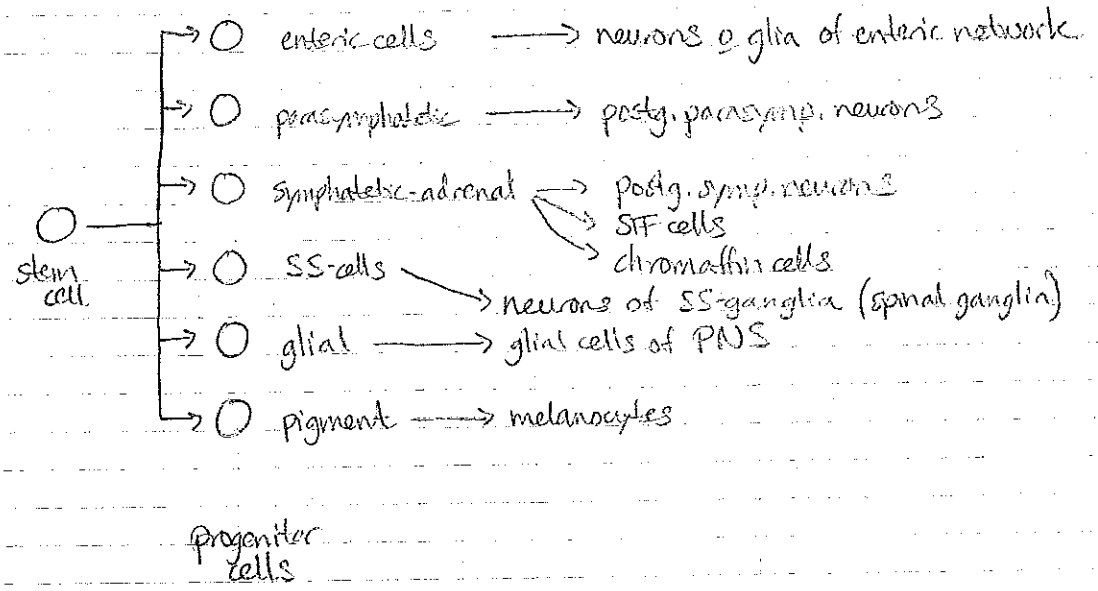
Then forebrain + hindbrain differentiate so 5 secondary vesicles arise:

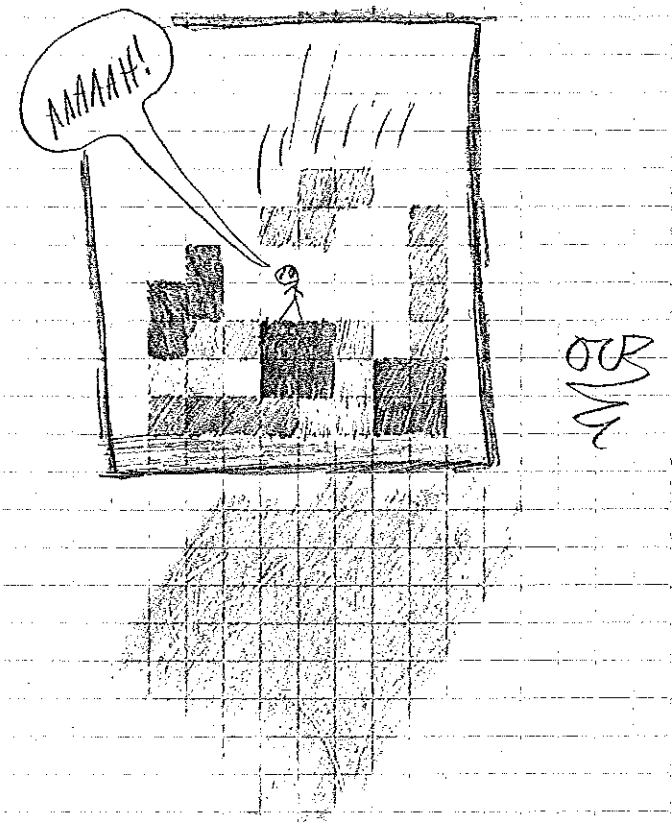
Forbrain → telencephalon
→ diencephalon

Midbrain — mesencephalon

Hindbrain → metencephalon — pons, cerebellum
→ myelencephalon — med obl.

Derivatives of neural crest




AAAAAH!
OUR