PHYSIOLOGY OF THE STOMATOGNATHIC SYSTEM IST MIDTERM NOTES (2018)

UNITS 1-2: Cranial Nerves

-Cranial Nerve **I** is the **Olfactory** Nerve -> Special Visceral Afferent (**SVA**) fibers
-SVA fibers sense **taste** and **smell**.

-Cranial nerve **II Optic** Nerve : sensory only, **SSA** fibers.

Eye Movement:
-Cranial nerves **III,IV,VI**: **motor** nerves **only**. responsible for **movement** of the **eye**.
-movement of the eye not always voluntary, thus we will have both somatic and autonomic innervation. -some movements are reflexes.
-**Skeletal** muscles move the eye: **somatic** motor neurons.
-Movement: up,down,lateral and medial -> We need **4 muscles**. They have the shape of a rect line (hence the name rectus). *superior,inferior,lateral,medial:* Common **origin -> annulus of zinn.**
-each one of them joins one side of the eyeball. *for some oblique movements we need two oblique muscles. (superior and inferior oblique muscles)*.
rectus: oblique line from annulus of zinn to eyeball. oblique: oblique line.

-superior oblique muscle goes next to the bone and then reaches one region which is fibrocartilage (trochlea, joins the bone), region where muscle attaches and then makes a turn. (hence oblique). -trochlea gives the name to the nerve that innervates this muscle (**cranial nerve IV -> trochlear. innervates superior oblique.**)

-we have 6 skeletal muscles for the eye: 4 rectus and 2 obliques.

-**smooth muscles**: for the constriction of the pupil. **autonomic motor neurons** which innervate two areas in the eye -> iris and the lens. (cristalline that we use for focusing). both of them stretch or relax through smooth muscles.

-I,II only sensory. III,IV,VI only motor (red painted fibers).

-**III,IV,VI** have general somatic **efferent** fibers (**GSE**).
-oculomotor nerve (III) also carries visceral information because it has a branch of the parasympathetic nervous system. (**GVE**)

-*there is somatic and there autonomic nervous system -> it's divisions: sympathetic and parasympathetic.* opposite so nerves coming from different regions. the **sympathetic** nerves come from **thoracic** and **lumbar** regions of the **spinal cord** and the **parasympathetic** come from the **extremes**, **sympathetic nerves** are in the **spinal cord** while **cranial** must be **parasympathetic**.
-there are **4/12 cranial nerves** that carry **parasympathetic** information. **cranial nerve III (oculomotor) is one** of them.

-GSE fibers are for somatic skeletal fibers and **GVE** for **smooth muscle** (ciliary and iris). cranial nerves IV,VI only GSE.

visceral= autonomic, involuntary. (e.g. smooth muscle,glands,cardiac muscle). -general visceral fibers which could be sensory or motor (afferent or efferent). autonomic can be both sympathetic and parasympathetic. somatic= voluntary, innervates skeletal muscles. efferent= motor

-in the case of oculomotor nerve they are efferent cause the motor information is for the smooth muscle in the iris and in the crystalline.

Origin of cranial nerves III,IV,VI:
-**Midbrain**: origin of **III (oculomotor),IV (trochlear)**.
III -> anterior midbrain. IV -> posterior midbrain, but then goes towards anterior.
-cranial nerve **VI (abduscens)**: in the **pons**.

-for the abduscens inside the pons, the axon leaves the **superior orbital fissure** (as well as other two) to reach the eyeball.
-part between pons and medulla: pontomedullary junction. (where the abduscens is)

[when we paint the neurons the little dot is the soma, and the line is the axon.
***motor neurons** are **multipolar**. -nucleus: accumulation of somas of neurons in the cns*
*gray matter: accumulation of **somas** of neurons/nuclei in the **cns**.*
***axon** of neuron **crosses white matter**.]*

-Annulus of zinn: some cross it inside and one is lateral to it.

-Oculomotor (III) is a motor nerve, leaves **anterior aspect** of midbrain, goes and extends anteriorly and then it **branches** into two: **superior** and **inferior branches**. (with respective parts of the eye). **both parts cross the annulus of zinn**.

-Optic Nerve is cranial nerve II, **crosses** the **sphenoid bone** through the **optic canal**. -all the others for the eye cross through the superior orbital fissure.

-Oculomotor nerve (III) has **two branches:** superior and inferior. both are skeletal. *it doesn't function to distinguish color.*
-the **superior branch** innervates the **superior rectus** and the muscle that moves the upper eyelid (voluntary movement) which is the **levator palpabrae superioris**..
the **inferior** branch innervates **three muscles**: **medial rectus, inferior rectus, and inferior oblique**.

[on the other hand the superior oblique muscle is innervated by the trochlear nerve (IV) cause it has the trochlea. and the lateral rectus by cranial nerve VI abduscencs.] (*these are all skeletal muscles, but the oculomotor nerve also has parasympathetic info).*

-in the autonomic nervous system **ANS** we need **two neurons** to **synapse**. the synapse happens **in** a **ganglion**.
-when you see a **ganglion** it's either **sensory** or **parasympathetic** information.
in **motor neurons** we only need one neuron: from the cns to the skeletal muscle. they **don't synapse in a ganglion**.

-the **oculomotor** nerve gives off **parasympathetic** fibers to the **ciliary ganglion**.
-**parasympathetic** information to the **ciliary muscle** and to the **iris** towards the **crystalline** and for the **pupils**. the ganglion comes from the **inferior branch of the oculomotor nerve (III)**.
-if the **somatic** motor neurons are affected we can't control the **movement** of the eye, if the **parasympathetic** fibers are damaged the **size** of the **pupil** will change.
-when you rest and digest (**parasympathetic**) the pupils are **constricted**. when you instead are in a dangerous situation your body wants to get much light as possible to see better -> pupil **dilation** (**mydriasis**) -> **sympathetic** response.
-if cranial nerve III (**oculomotor**) **doesn't work** you get **pupil dilation**, cause normal function is to constrict.
-so to check functioning you need to check pupil size, the response to light, and the movement (eye tracking). -you also check the eyelid (cause superior **eyelid** innervated, if it **doesn't work** it **will drop**).

IV, VI only somatic motor neurons and **only innervate one muscle**.
-trochlear (IV) innervates **superior oblique**, and crosses superior orbital fissure. it is the **only one that doesn't cross annulus of zinn**. it is lateral to it.

-Abduscens nerve (VI): **crosses** the **annulus** of **zinn** and **innervates** the **lateral rectus**.

-**damage** in **trochlear IV** we lose control of movement of eye (**double vision**…) **will go towards medial** part of body. similar for **abduscens VI damage**, we lose control of somatic movement of the eye, we will **cannot rotate it**.

ganglion: accumulation of somas of neurons outside the cns. here there will be a synapse with the axon terminal of another neuron. it may be a place where two sensory neurons synapse (sensory neurons are unipolar or bipolar).
ganglions are only parasympathetic or sensory, never somatic motor.
the ciliary one is parasympathetic, comes from the inferior branch of the oculomotor and synapses with another motor neuron which goes to the cristalline and iris.

-Vestibulocochlear (VIII):
-**sensory** only, special sense afferent (**SSA**) **fibers**. same fibers as cranial nerve II (optic). I (olfactory) is special visceral afferent (SVA).
-external ear: we don't have the ossicles. there is a little bone that we use to send the vibration from the tympanus towards the inner structure of the ear.
vestible: has 3 rings in different directions, used for **equilibrium**.
cochlea: looks like a snail, used for **hearing**.
-nerve has **two branches**, one comes from the cochlea and the other from the vestible. the join together and form one nerve, but with double sensory information. (equilibrium and hearing).
-origin: **lower** border of **pons** and **anterior** part of medulla oblungata -> **pontomedullary junction**.
-crosses the **posterior cranial fossa** and **enters** the **acustic internal meautus** and join the vestible and cochlea. it goes **together with the facial nerve** at that moment.
-you test if it's working by doing hearing or balance test, asking person to walk in a straight line.
-if **damaged** you could be deaf or experience dizziness and nausea and **nystagmus**: involuntary condition which leads to uncontrolled movement of the eye. nystagmus is not a defect of a motor neuron (cause VIII is sensory, even though it is a motor response.) -this occurs because it synapses with gray matter (where all the synapses occur) with many different centers of the encephalon. III,IV,VI are responsible for the movements of the eye and they receive info from one nucleus in the vestible. (from cranial nerve VIII). this is why for the movement of the eye we also react to things we listen. so if VIII is damaged we have also a problem with eye movement since they synapse.
(e.g. when you hear something with your right ear, the info reaches your left cerebral cortex. we have a reflex to move our head when we hear a big fulminant noise because involuntarily the neurons synapse with others which go to other places.)
-same principle with olfactory nerve (sensory only): when you smell food you begin salivation because it synapses with centers that control salivary glands.
so cranial nerves might only be of one type but they make connections with other areas in the brain, triggering a response.

-Vagus nerve (cranial nerve X):
-origin in **medulla oblungata**. it is both sensory and motor (**mixed**). it is **one of the four** nerves that carries also **parasympathetic** information. (both sensory and motor)
-we have sensory somatic innervation and sensory autonomic and same for motor. this is the reason for which it has **4 nuclei**: **solitary**, **ambigous**,**dorsal** and **spinal trigeminal**).
nuclei: somas of interneurons that make decisions. the axons may be afferent or efferent.
-has **two ganglia** -> **superior** and **inferior**.
-the nerve **crosses** the **jugular foramen together with the cranial nerve XI**. in each side of the jugular foramen we find the ganglion.
-has 5 types of fibers:
-**SVE** fibers: special visceral efferent. come from the **ambiguous** nucleus, innervate some **involuntary muscles** (larynx,pharynx,soft palate and the palatoglossal muscle of the tongue). beginning of **swallowing reflex** is voluntary but the end is **involuntary**. (where the **SVE** kick in). [food and air intake]

-**GVE** fibers: **general** visceral efferent. -comes from **dorsal** nucleus. -refering to heart, lungs, gi tract. (lower heart rate, bronchoconstriction, better digestion)
->smooth muscle, glands, **parasympathetic** innervation.
-vagus is always parasympathetic but has both afferent and efferent fibers.
-**GSA** fibers: sensory neurons. (afferent) -**spinal trigeminal nucleus and upper ganglion** -from dura mater of posterior fossa **meninges** and posterior side of the external side of the **ear** and again from **pharynx** and **larynx**.
-**SVA** fibers: **solitary tract nucleus**. only **smell** and **taste**. -epiglottis taste buds
-**GVA** fibers: **inferior ganglion** and **solitary tract nucleus**. -**sensory**, **parasympathetic info** from the heart: **baroreceptors** from **arch** of **aorta**, carotid sinus, chemoreceptors, stretch receptors in the intestine, ph receptors in stomach, **receptors** of **mucosa** of **pharynx** and **larynx**.
-GVA and GVE are parasympathetic.
-when you follow the ganglia (superior and inferior) from the jugular foramen they innervate pharynx, larynx, reach the heart, bronchi, stomach and also the small intestine (beginning and middle part)

Cranial nerve XI: Accessory.
-accesory cause **helping** the **vagus**, it is **motor, GSE fibers.**
-comes from the **spinal cord ->** not considered a real cranial nerve.
-it innervates two skeletal muscles: **sternocleidomastoid** and **trapezium**.(somatic)
-why considered a cranial and not spinal:
-**spinal nerves** leave to the **right** and **left** and they are all **mixed**.
-**accessory** instead **leaves from the 1st 5 cervical regions** of the spinal cord and it's motor (**not mixed**).
-the **fibers** instead of going to right and left following the spinal nerves **go up to cross** the **foramen magnum.**
-the nerve has **two roots**: one in the **spinal cord** for the **skeletal muscles** and one in the **pons** (cranial). -the roots come together **with** the fibers of the **vagus** nerve **next to** the **jugular foramen**, they **look** the **same** and **go to** the **same organ**: the **larynx**.

-protrusion of tongue is made by hypoglossal nerve (XII)

S: sensory M: motor B: both
Some Say Marry Money But My Brother Says Big Boobs Matter Most.

UNIT 3: Trigeminal Nerve

-trigeminal nerve is cranial nerve **V**
-it's named trigeminal because it has **3 main branches**:
v1 (opthalmic) v2 (maxillary) v3 (mandibular)
-origin-> **pons**. (means bridge, region where we make connection of axons, some of them go into the cerebral cortex but some others join the cerebellum, since we have this crossing it's like a bridge, area where we receive axons going into different directions).
-it is a **mixed nerve**, both sensory and motor. not all the three branches are mixed. the sensory (afferent) neurons are in all 3 branches, but the motor neurons (efferent) are only in the the mandibular v3.
-it doesn't carry parasympathetic information!
-we receive sensations from a very broad area of the skin (all of the face, **middle** of the skull,,)
-by this we mean dermatome: region of the skin.
-we receive a lot of fibers, we might sense: **touch, temperature, pain, proprioception**.
-a **proprioceptor** gives information on **position** of the **muscles**, in this case **of** the **face**.
-**sensory** neurons -> **GSA** (general somatic afferent),all the three branches.

-in the **mandibular branch** we have the **muscles** of the **face**, **involved** in **chewing**. (**skeletal** muscles but **not all of it is voluntary**). thus they are **not** GSE (general somatic efferent) but special because there is a way of **controlling** the **contraction** which is **not completely voluntary** and is related to digestion. **-SVE fibers -> special visceral efferent.**
-teeth pain (GSA) comes from the trigeminal.
-proprioceptors are in muscles and joints.
-***dura mater: meninges***. *(arachnoid, pia mater) it's a type of* ***connective tissue****. used to* ***protect*** *encephalon.* ***in between*** *the meninges we have* ***spaces*** *(epidural,subdural,subarachnoid). in between two of meninges we have the* ***csf*** *(cerebrospinalfluid). in between the* ***subarachnoid****. this fluid gives both protection and* ***nutrients****. -there may be some parts of the cranial nerves covered by csf. -all connective tissues with the exception of cartilage are innervated and vascularized.*
*-mucosa (****epithelium****) are* ***not innervated*** *but the* ***connective tissue*** *behind* ***is****. we have receptors in the mucosa for touch,pain, temperature… (nasal cavity, oral)*
-in some regions we will have branches which are coming from other nerves.
-from the origin of the nerve they keep branching and branching until they reach target organs.
-one of the **branches** is the **lingual nerve**. if you look at it you see several groups of axons of neurons with connective tissue around, but also see **branches of the facial nerve**. (different nerves originally but the branches meet at some point). the **trigeminal** nerve **doesn't have parasympathetic** fibers but together with this branch of the facial nerve we have innervation of the **salivary glands** (which do **have parasympathetic info**). -the **branches** of the **nerves run together**, but the **axons never mix** because they are covered by their own connective tissue. they just join together to go in one particular area. branch of VII goes next to a branch of V, happens a lot, easy to get confused.

-**sensory neurons** are **bipolar** or **unipolar**, meaning the **soma** is in the **middle** and in **one side** we have the **dendrite** and in the **other side** we have the **axon**. *-the soma is the dot and the line is the axon. at the axon terminal when you see a "V" with a dot, it means there is a synapse.*
-where the somas of all the sensory neurons come together (accumulation of somas of neurons outside the cns) -> ganglion. -the trigeminal **ganglion** is common for **all** the **three branches**, it encloses the **somas** of all the sensory neurons of the 3 branches.
-there is nucleus for **motor** info of the **mandibular branch**.
-parasympathetic fibers coming from facial nerve. (VII) this fibers reach the mandible, going together with the fibers of the trigeminal. branch of trigeminal **collateral** to branch of facial.

-areas which are receiving sensory info from trigeminal: skin, dura mater, paranasal sinuses, oral mucosa, mucosa of the nose…
-sensory neurons sense pain,temperature,touch,proprioception (**4 types of neurons**). they need to synapse in the central nervous system with another neuron that can understand the information.
-**synapse** in the **central nervous system** occur in the **gray matter**. (accumulation of somas of neurons in the cns -> nucleus/nuclei.)
-the **sensory neurons of** the **trigeminal** nerve synapse with **three sensory nuclei** in the **cns**.
-pons also contains axons that go the **cerebellum** (posterior to the brain stem) which is responsible for **equilibrium**, they attach to the cerebral peduncle. (towards posterior).

-in the **midbrain's posterior part** there are **4 little bones** (**quadrigeminal tubercles**: **superior and inferior coliculi**) which **are always posterior**. (way to recognize if anterior or posterior view)

-**spinal nerves** have **two roots**: a **ventral** and a **dorsal**. sensory and motor info travel separately, one root for one and one for the other. **dorsal/posterior: sensory** ; **ventral/anterior: motor.**

-the **sensory nucleus** is much **bigger** cause we receive info from the 4 different neurons.
-we have **3 sensory nuclei that connect to each other:**
1 -the **principal nucleus** is in the **pons**. -receives info from **touch** of the face
2 -the **mesencephalic** nucleus is in the **midbrain** (*between midbrain and pons*) -receives info for **proprioception**.

3 -the **spinal** nucleus is a really long nucleus that **starts in the pons, runs towards the medulla oblungata and joins the first regions in the spinal cord**. -receives information of **pain** and **temperature.**

-the **motor** nucleus is really **small**, it contains the **somas** of **motor neurons** innervate the **muscles** of **mastication** and some other muscles. -consists of **SVE** fibers. (special visceral efferent).

-**supratrigeminal** nucleus: **doesn't belong to trigeminal nerve**, cause that only haves 3 sensory and 1 motor.
-it is **superior to** the **trigeminal motor nucleus**, and is a **nucleus of interneurons** which **receives signals** from **proprioceptors** and **sends signals to motor nucleus involved in the muscles of mastication**.
-so there are synapses between them, it can control in an involuntary way these skeletal muscles. this is thus the nucleus which **generates the involuntary pattern for the muscles of mastication.**

-vagus nerve also innervates a little part of the ear, not the trigeminal.

-muscles of mastication: **temporalis**, **masseter**, **lateral** and **medial pterygoid**, **mylohyoid** (attachment for the muscles of the tongue), **digastric** (used to move the tongue during swallowing)
-the digastric muscle's anterior belly belongs to the trigeminal as for innervation but not the posterior belly.

-**palate** has two main muscles -> **tensor veli palatini** (innervated by CN V) and **levator**.

-**tensor tympani** muscle (stretches the membrane of the **inner ear** (tympanic membrane) in order for it to **vibrate in response to** the **sound**.)
-thus, **damage** in the **mandibular branch** would **lead** to **ear damage** too, because the tensor tympani muscle is innervated by it.

-**anterior 2/3** of tongue **innervated** by **trigeminal**.
-trigeminal neuralgia: horrible pain sensation due to damage to the sensory neurons of the trigeminal.
-**problem** in **trigeminal** also could lead to **problems** in **temperature discrimination**.

Trajectory:
-trigeminal nerve **exits laterally in the pons**, large sensory root, small motor root. **located in posterior cranial fossa**. -the **ganglion** contains the **somas** of the **sensory neurons** only!!!
-we start laterally in the pons and **move towards the tentorium cerebelli** (connective tissue fold between cerebrum and cerebelli). (falx cerebri is one of the 3 folds of the dura mater and goes in between the two cerebral hemispheres) (falx cerebelli between the two cerebellar hemispheres).
-then we **enter the superior portion of the petrous part of the temporal bone**, region with small **depression** that **holds** the **trigeminal ganglion**-> **trigeminal or gasser's cave.**
-it then **keeps moving** into the **middle cranial fossa**, **branches into three** and then **each of the branches exit through a different foramen**.
-the ganglion is **lateral and SUPERIOR respect to the internal carotid**, **inferior to the temporal lobe**. -it's also **lateral to** oculomotor, trochlear and abduscens nerves. (III,IV,VI)
-the **motor root** of the trigeminal nerve passes **inferior** to the trigeminal ganglion, it is **collateral** to it, doesn't enter in it.
-layer to **protect** the trigeminal ganglion is a **fold of dura mater** which surrounds **one part** of the ganglion with the **subarachnoid space** (**with** the **cerebrospinal fluid** going through it).
-**meckel's cave**, which is **one portion in which the trigeminal ganglion is surrounded by csf**, not entirely thus it is not the same as the trigeminal ganglion. it covers the **root** of the nerve **till half** of the ganglion more or less.

-**opthalmic branch** (V1) goes to the **eye** -> **crosses the superior orbital fissure** (in the sphenoid). together with the abduscens and oculumotor, which **cross the annulus of zinn**. also the trochlear nerve goes towards the superior orbital fissure but it is lateral to the annulus of zinn.

-**maxillary** (V2) branch exits through **foramen rotundum**.
-**mandibular** (V3) branch exits through **foramen ovale**.

-seeing quadrigeminal tubercles and the two peduncles in the pons indicate it is the posterior brain stem.
-laterally in the pons the trigeminal nerve begins

-we have ascending and descending pathways. pathway: sequence of neurons that send information through a place. sensory neurons send info to the cns. (ascending). ***the sensory neurons synapse two times, so we need 3 neurons****. (even in a cranial nerve) we call them primary, second and third order neurons. the* ***primary is the first to receive the sensation****.* ***in the thalamus we have two neurons, one on each side****.* ***thalamus -> gray matter (nuclei)****, we have* ***interneurons*** *and synapses between the* ***axon terminal*** *of a* ***neuron*** *and the* ***soma of another****.*

-**pain** will send info the **spinal nucleus**. *the primary order neuron (which could be from any of the three branches of the trigeminal (v1,v2,v3) synapses by the axon with an interneuron of the spinal nucleus. (second order neuron) -the* ***soma*** *of the* ***primary order neuron*** *is in the* ***ganglion****, the* ***soma*** *of the* ***second order*** *neuron is in the* ***nucleus****.*
soma *->* ***gray matter****;* ***axon*** *->* ***white matter****;* ***accumulation*** *of* ***axons*** *of neurons in the* ***cns*** *->* ***tract***
-the soma of the second order neuron is on the **same lateral side where we receive information**, but the axon crosses to the other side to the thalamus. we synapse with the third order neuron in the thalamus **in the other side**, meaning if the information is coming from the right side of the skin of the face it will arrive to the left thalamus. -this is known as the trigeminal-thalamic tract (not a nerve, inside the cns, white matter).
-the **third order** neuron goes from the **thalamus** to the **cerebral cortex**, where we receive the sensation.
trigeminal reticular fibers: network.
-brain stem contains medulla oblungata, midbrain, and pons.

UNITS 4-5:

-**trigeminal ganglion** purely sensory, purely cause **no parasympathetic fibers** and no motor too. there are **no synapses in this ganglion**, there are **just the somas**. we **synapse** in one of the **sensory nuclei** of the trigeminal: mesencephalic, principal (pons), spinal nucleus.
-not all ganglions are the same. e.g. **ciliary ganglion**, arises from the synapse of the inferior branch of the oculomotor nerve. it is **sensory**, innervates **ciliary muscle** which is responsible for **cristalline** contraction and relaxation, and the **lens** in the eye we use for focusing. also innervates the **muscles** in the **iris** so we can have **pupil dilation or constriction** -> **involuntary** -> **parasympathetic ganglion**. (fibers of the oculomotor nerve) **we have synapses** in the ganglion because in a parasympathetic system we have a **pre-ganglionic neuron** and a **post-ganglionic neuron**. some of the sensory fibers from the trigeminal nerve cross this ganglion. (cross but don't synapse) so when you look at the ciliary ganglion you see **parasympathetic fibers** come from the **oculomotor** nerve, while the **sensory fibers** come **from** the **trigeminal** nerve.
-sympathetic ganglions **exist** but not in the head and neck because **sympathetic** is **only** in the **spinal division**. but a ganglion in the head and neck might receive the **axons** of sympathetic neurons. (but they **aren't** the ones that synapse).

-Ophthalmic (V1) branch:
-most superior, **shortest of the three branches**. only sensory!
-trigeminal ganglia is located in trigeminal cave/gasser's cave in the petrous aspect of the temporal bone and is surrounded partially by csf in the meckel's cave. then it will run **lateral in** the cavernous sinus.
-dermatome: area of the skin which receives innervation from the same nerve.
-opthalmic dermatome: skull, forehead,eyelids, **upper** part of nose. remember this **doesn't just include the skin** but all the structures underneath (dura mater, nasal cavity…)
-nasal cavity: we just receive sensations from the **upper part** (beginning/**most anterior part**: frontal sinus,ethmoidal cells,falx cerebri), the rest accounts for the maxillary branch.
-conjunctiva: connective tissue around the eyes where we have blood vessels.
-lacrimal gland is innervated too but since only sensory there are **not neurons that induce** the **secretion**. we might have neurons from other nerves though.
-falx cerebri,falx cerebelli, and tentorium cerebelli all are connective tissues innervated by it. so are the upper eyelid, dorsum of the nose, lining mucosa of the upper part of the nose (because the rest is innervated from the maxillary), air cells and anterior part of scalp.

-oculomotor **III**, trochlear **IV**, abduscens **VI** (*motor nerves for the eye*) **all go through the cavernous sinus** as well. 7 nerves in total go through it. so do the maxillary and opthalmic branch of trigeminal. (**not** mandibular). maxillary and opthalmic are towards it's lateral wall and inferior.

-Ophthalmic (V1):
-**crosses cavernous sinus**, then **branches into 4:**
1) **meningeal** (innervates **meninges** and **dura mater**) is the first and really **small.**
2) **frontal** (for the frontal bone)
3) **nasociliary** (for **upper** nasal cavity and **ciliary ganglion** [*parasympathetic ganglion of the oculomotor nerve which receives sensory neurons that cross the ganglion without synapsing* and may receive touch signals from the eyeball such as getting something in the eye]
4) **lacrimal** (to the **lacrimal gland**) branch.

ciliary nerves: we have **short** (closer to the eyeball) and **long** (farther from the eyeball). these branches further branch.

-the **opthalmic** division goes **through** the **superior orbital fissure**. damage to this division does not give blindness. (damage to the optic nerve [II] does.)

-annulus of zinn: **tendon** in shape of a ring where the **4 muscles** that reach the eyeball are found [superior and inferior,medial and lateral rectus]

-optic canal (sphenoid): for optic nerve (CN II).
-oculomotor has superior and inferior branches, they both cross the annulus of zinn.
-trochlear: reaches the fibrocartilage on one side of the orbit which is used for the superior oblique muscle to make a u-turn. the trochlear nerve is lateral to the annulus of zinn.
-abduscens: also inside, it crosses the annulus of zinn.

1-**Meningeal** nerve branch: **next to** the **cavernous sinus**.

-the **nasociliary branch crosses** the **annulus** of zinn together with the two branches of the oculomotor nerve III and the abduscens VI.
-**lateral** nerves to annulus: **frontal**, **lacrimal** and **trochlear**. (don't cross it, they are lateral to it and not internal).

2-**Frontal** nerve branch: reaches the **frontal bone**, goes **through** to the **superior orbital fissure** but **lateral** to the **annulus** of **zinn** (doesn't cross it). will **branch into two** as it moves towards anterior: **supraorbital** and **supratrochlear**.

-**supraorbital** (will **cross** the **supraorbital notch/foramen)**will record info from a part of the **forehead**, **scalp,** with the exception of the more **medial** part of the **upper eyelid** and **root** of **nose** will go through the **supratrochlear**.
-**both** supraorbital and supratrochlear innervate the **conjunctiva**. (receives innervation from many different branches)

3-**Nasociliary** nerve branch: innervates **nose** and **eye**. passes **through superior orbital fissure**.
-there are both long and short ciliary nerves.
-**crosses** the **annulus** of **zinn**. **sensory neurons** coming **from** the **eyeball** cross the ciliary ganglion without synapsing and then **join** the nasociliary nerve.
-short nerve when they are close to the eye, long when they reach it laterally.
-we will **reach** the **ethmoid** **anteriorly** and **posteriorly by the anterior** (terminal) **and posterior** (collateral) **ethmoidal nerves**. there is also an **infratrochlear** (terminal) nerve. (branch of the nasociliary opposed to **supratrochlear** which is a branch of the **frontal** nerve)
-**ciliary ganglion** is more **anterior** and **lateral to** the **annulus** of zinn, it's the place where we **receive the long and short ciliary nerves**: they cross the ganglion and reach the nasociliary nerves.
-**anterior ethmoidal** passes through the **anterior ethmoidal foramen**, receives sensory information from the **meninges** of the **anterior cranial fossa** and the **anterior part** of the **nasal cavity**.
-**posterior ethmoidal** passes through the **posterior ethmoidal foramen**, receives sensory information from the **ethmoidal air cells** and **sphenoid sinus**.
-**infratrochlear**: passes through **medial commissure of the eye**, inferior to the trochlear nerve, innervates the **skin of the eyelids, side of nose, conjunctiva again, lacrimal sac and nasolacrimal duct**. (but not related to the secretion, cause sensory nerve only).
-nasociliary nerve includes: **anterior ethmoid** nerve, **external nasal** branch of the anterior ethmoid and the **septal branch** of the anterior ethmoid. only the **most anterior** and **superior**, the rest belongs to the maxillary.

4- **Lacrimal** nerve branch: **lateral to** the **annulus** of zinn because will **reach** the **lacrimal gland** which is lateral. it doesn't stop at that level. it **keeps moving forward**,there is a **medial branch** that finishes in the **skin of the upper eyelid**.
-the **lateral branch** of the lacrimal nerve **finds** a **branch of** the **zygomatic** nerve (belonging to maxillary but reaching the same region [lacrimal gland],careful).
-also crosses superior orbital fissure.

Maxillary branch (V2):
-it **passes through** the **lower part lateral wall of the cavernous sinus.** only one that doesn't is the mandibular division of the trigeminal.
-we have sensory fibers (pain, temperature,touch,proprioception) coming from the skin of the face between the **palpebral fissure**, the mouth, nasal cavity (except roof and most anterior part), and from the maxillary teeth.
-leaves through the foramen **rotundum**. **before we enter** the **foramen rotundum** there is a branch: **meningeal** (there is both an opthalmic meningeal branch and a meningeal branch from the maxillary). they both innervate the dura mater (receptors from both of them).
thus not part of the pterygopalatine ganglion/fossa.
-collateral branches: meningeal, zygomatic, branches to and from the pterygopalatine ganglia
-terminal branch: superior anterior alveolar branch
-after the foramen rotundum we **reach** the **pterygopalatine fossa**, where there is a **pterygopalatine ganglion**. we have **sensory** neurons in it. we have parasympathetic fibers that synapse in this ganglion but they don't belong to the trigeminal.
-there will be nerves that join the pterygopalatine ganglion and nerves that don't. (they just join the maxillary nerve by themselves). *important to know which ones do and which don't*.
big opening: fissure ; regular size: foramen ; small: canal
-we have **two fissures** -> for entering fibers from the eye (**inferior orbital fissure** and **pterygomaxillary fissure**)

-we have **two foramina** -> **sphenopalatine** foramen and **foramen rotundum** (through which the nerve crosses)
-**canals** -> **pharyngeal**, **vidian**, **pterygopalatine**
-**orbit of eye**, maxilla, nasal and oral cavity innervated. some fibers receive sensations but before they reach the maxillary nerve they have to cross the ganglion but some others don't cross (e.g. **zygomatic** nerve which **joins directly the maxillary nerve**)
-from the **inferior orbital fissure** we get the **zygomatic nerve** and it reaches the maxillary nerve.
-**infraorbital** nerve complicated, **doesn't join** the **ganglion**.

-**nasal cavity**: *nasopalatine nerve (from nose and palate), crosses the **sphenopalatine foramen** and **joins** the **ganglion** (goes **across the roof** of the nasal cavity, **reaches the nasal septum** and then goes **downward, oblique and forward** [innervating the region the opthalmic didn't reach]).
-it is part of the sensory root of the mouth **through the incisive canal** (comes out through the incisal foramen) which it crosses and communicates with the other nerve from the other side. the pain in the **gums** from this region is going to be recorded in this nerve. (nasopalatine)
-thus innervates: structures in the **palate**, around **upper central** and **lateral incisors**, and the **canines**; and the **mucus membrane of** the **nasal septum**. (nerve of interest for dentists.)
-we also have ***inferioposterior nasal branches** (**posteroinferior** lateral nasal nerve) and **posterosuperior nasal branches**. (**posterosuperior** lateral nasal nerve). not the anterior ethmoid cause belongs to opthalmic. these two branches also **run through the sphenopalatine foramen** to reach the **nasal septum** and then we have **two brances**: **upper posterior part** and **lower posterior part** of the **lateral wall** of the **nose**. (go **through** the **conchae**: protrusions on the sides of the nasal cavity which are covered by mucous membrane and they receive also sensory neurons).

-***pharyngeal** nerve branch: it is the **most posterior to the ganglion** and **crosses through** the **palatovaginal** canal. for the pharynx (**nasopharynx**), **crosses the pharyngeal canal** and **joins** the **ganglion** and then the maxillary nerve.

-**oral cavity**: **greater** and **lesser palatine nerve**, both **cross** the **greater palatine canal**, **join** the **ganglion** and then the nerve.
-lacrimal nerve doesn't belong to the maxillary division but to the opthalmic.

-**zygomatic** nerve has **two branches**:
zygomaticofacial (skin of **cheek**) and **zygomaticotemporal** (skin of **temples**).

-the parasympathetic fibers that reach the pterygopalatine ganglion arrive from the petrosal nerve. (mixed ganglion but only the sensory neurons are the ones that belong to the maxillary branch)

-there are **6** different **branches** that go **to and from** the **pterygopalatine ganglion**.
* = 3 branches go **towards posterior**: **pharyngeal**, **nasopalatine**, **posterior lateral nasal** (inf and sup)

-when you go **from** the **ganglion towards inferior** you find the **greater palatine nerve** (**most anterior**, innervates **hard palate**) and **lesser palatine nerves**,(**soft palate, ugula,tonsils**)
-they both go through the **greater palatine canal**. supply also the **lining membrane of the nasal cavity**. -the greater palatine is much longer cause receives sensation from a bigger area (hard palate).
-for the greater it descends through the greater palatine canal, we come out through the greater palatine foramen and **we move anterior** to supply the hard palate.
-the **lesser** palatine nerve goes through the greater palatine canal, **leaves through** the **lesser palatine foramen** and we **go towards posterior** instead of towards anterior.
-for the **lesser** palatine we have **two branches**: **middle and posterior**, we reach the soft palate in both the anterior and posterior part (reason for two branches). the middle lesser palatine innervates the **mucosa** of the **third molar** as well. for the posterior the **isthmus** of the **fauces**.

-pterygopalatine ganglion receives neurons that receives neurons from both parasympathetic and sympathetic nervous system (which don't belong/come from the trigeminal nerve but they join in the ganglion)

when you eat something very cold sometime you experience headache immediately because of the **greater and lesser palatine nerves** (which are sensory GSA). they activate and send signal to the brain which responds by increasing vasodilation in the blood vessels around this area. (temperature of blood is 38°C, so by vasodilation we want more blood to arrive to the area to try to warm it) since the **vasodilation** occurs **immediately** there's pain, easily could be avoided by eating less cold things, having them longer in the mouth before swallowing etc. pain lasts around 30 secs.

vidian canal: where we receive the fibers that don't belong to the trigeminal nerve, where we receive the **parasympathetic fibers** coming from the [greater petrosal] **facial nerve** (**VII**). it synapses in the ganglion with the **post ganglionic** neuron. (which then might reach many different places [lacrimal,salivary,palate,nose: many different places where they **influence the secretion**].) it will go to the **lacrimal gland**.
-**sympathetic** fibers in the vidian canal come from the **deep petrosal nerve**.
-all of them join in the **pterygopalatine fossa** where we have the ganglion.
-neurons that receive parasympathetic and sympathetic information have a secretory function.

-in the **autonomic** nervous system we need **2 neurons** (from the **cns** to the **target organ**).
we always talk about **pre-ganglionic** and **post-ganglionic**.
ganglion: accumulation of somas of neurons **outside** the cns
pre ganglionic neuron coming from the facial nerve comes from the brain stem and reaches the ganglion where they synapse with the post ganglionic neuron (which targets the same organs that we have seen in the trigeminal -> lacrimal gland,nasal cavity, nasopharynx, palate)
secretion is not sensory, it **responds to sympathetic and parasympathetic**.
most superior salivary glands is the parotid.

*-**sympathetic** nerves are always the **spinal** nerves, they come from **thoracic** and **lumbar** regions of the **spinal cord**. so sympathethic pre ganglionic neurons come from the spinal cord, there are **no cranial nerves** that **carry sympathetic information**.*

this pre ganglionic neuron synapses in a **ganglion** which **may be anterior or lateral to** the **spinal cord**. **from this** ganglion the **post ganglionic** neuron **reaches** the **pterygopalatine ganglion**.
-**deep petrosal** nerve (**sympathetic**), **branch** of the **spinal** nerve.
-sympathetic not from facial nerve but reach same place, even though fibers receive orders from different regions in the cns.
-the **parasympathetic synapse in** the **pterygopalatine ganglion** while the **sympathetic** just cross it cause they **already synapsed** (**it's** already the **post ganglionic neuron**). even the **sensory just cross**.

-the **infraorbital** nerve (**doesn't join** the **ganglion**) has branches that are going to reach the **sensory part** of the **root** of the **teeth** -> superior alveolar nerves. (some of them are branches of the infraorbital but not all of them).
-it's gonna reach an area where we have the **infraorbital foramen**.
-has **two branches**: **anterior and middle** superior alveolar nerves.
-the other branch that goes down is the **posterior superior** alveolar nerve (sometime there are two), which is **not part of** the **infraorbital** nerve, just **branches** of the **maxillary**.
-when the maxillary nerve enters in the infraorbital canal it changes name to infraorbital nerve.
goes **through** the **infraorbital fissure**, **joins** the **infraorbital groove**, **leaves through** the **infraorbital canal** and reaches/**opens** at the **infraorbital foramen** in the face. from here will reach the **lower eyelid** (through palpebral branches), and also has nasal branches for the **nasal alae** and labial branches for the **upper lip**.
-**inside** the **maxillary bone** there are **two canals** (one for each) which give rise to the **anterior** and **middle superior alveolar** nerve. (part of the infraorbital nerve)

-**middle** (infraorbital) **superior alveolar** nerve is **not always present**. but we always have anterior (infraorbital) and posterior (maxillary)
-for the **posterior** branch sometimes we have one and **sometimes two**.
-even if we only have one all the dental pieces have innervation.
-we are gonna inject anesthesia in the areas that are always present.

-so now we have the **pterygopalatine fossa**, but we are not in the **ganglion** cause that's **more anterior**. -as we go down the tuberosity of the maxilla we are going to **enter through** the **alveolar canals** (**could be one** only too) the substance of the **bone**, and we are going to have **branches** which will go towards **anterior** which will **join** with the **middle superior** alveolar nerve which also has branches going towards anterior cause **joins** the **anterior superior** alveolar nerve.

-**posterior superior alveolar** nerve which is a **branch** of the **maxillary** reaches the **second** and **third maxillary molars** and **two of the three roots** of the **maxillary first molar**. (with the **exception of** the **mesiobuccal root**). they **enter through** the **apical foramina** and join all those structures (periodontal ligament, membrane of maxillary sinus, gingiva, maxilla, periosteum).
-the posterior superior alveolar branch reaches the most posterior part of the maxilla, and keeps branching and branching untill it **joins** the **middle superior alveolar** nerve. (highly innervated area).

-from the **infraorbital** nerve there are **two branches**: **middle** and **anterior superior** alveolar nerves.
-the **first** branch is the **middle superior alveolar** nerve (**not always present**), will send GSA fibers to the **mucosa** in **sinus**, **premolars** and the **remaining third** of the **mesiobuccal root** of the **first maxillary molar**, **maxilla**,**periosteum**,**gingiva**,**periodontal ligament**)
-anterior superior alveolar nerve: branch we see before the exit of the infraorbital nerve through the infraorbital foramen.
-will go down the **anterior wall** of the **maxillary sinus**, **dividing** into two branches **to reach** all the **incisors** and **canines** with again the **periodontal ligament**,**maxilla**,**periosteum**,**gums** etc.
-also has a **nasal branch** to the **lateral wall** of the **inferior meatus** (anterior part),very small. for the **mucus membrane** of the **floor** of the **nasal cavity**.

Mandibular division V3:
-**mixed** (both motor **SVE** and sensory fibers GSA). -carries **motor** fibers that derivate from the **first branchial arch**.
-dermatome of mandible, cheeck, **temples**, oral cavity, **external ear** (even though also receives other nerves), **tympanic membrane** and temporomandibular joint, **meninges** (dura mater).
-we have seen **meningeal branches in all of the 3 areas** of the **trigeminal**.
-mandibular division **exits through foramen ovale** and then **joins the infratemporal fossa**.
this is the **largest division** of the trigeminal. we have the **otic ganglion**.
-this ganglion is sensory (from trigeminal), parasympathetic and sympathetic (from others).
-**two roots**: one **sensory** and one **motor**. sensory is much larger. they **join together**. has many branches.
-very **little branch** from the **trunk** of the nerve (not from otic ganglion), before we reach the ganglion, called the **nervous spinosum**. it goes into the cranial cavity into the **dura mater**. **sensory** for **meninges**.
-**medial pterygoid nerve** **motor branch** is **superior** to the **otic ganglion** (doesn't come from it), from which we get the nerves that reach the **tensor veli palatini** and the **tensor tympani** and the **medial pterygoid muscle**.
-**branches from** the **trunk** divide into two: **towards anterior mainly motor** (4) or **towards posterior mainly sensory** (3). there are exceptions, hence mainly. and also branches that go to the otic ganglion:
-branches that go toward **anterior (4)** are mainly **motor** with the exception of the ***buccal nerve** which is **sensory**. other 3 are **motor**. we innervate the **lateral pterygoid, *masseter, temporalis** through the respective nerves. (deep temporal for temporalis)

-branches that go toward **posterior (3)** are mainly **sensory** with the exception of the **mylohyoid** nerve (for mylohyoid muscle which is **motor**). the other 3 are **sensory** -> ****auricolotemporal** nerve (ear and temporal skin), ****lingual** nerve (tongue), ****inferior alveolar** nerves (alveolar structures of the teeth).

-taste is not included in the trigeminal nerve, it will travel through the branches of another nerve. the lingual nerve thus is **not** for taste.

Anterior:

-***masseteric nerve** (anterior and motor) for the masseter muscle **arises from** a **superior branch** called **temporomasseteric**, because it goes next to the temporal bone. this **crosses** the **mandibular notch with** the **masseteric artery** (they go together) and then reaches the **deep** surface of the masseter.
-masseteric nerve is motor, gives off motor branches to the temporomandibular joint.
-temporal nerve -> temporal masseteric nerve -> masseteric nerve. (together with the artery) for the innervation and irrigation of the muscle.

-***buccal nerve**: (**anterior and exception -> sensory)** -the motor branch that crosses it is from the facial nerve (VII) while the sensory is from the trigeminal. (V) *from temporobuccal nerve.*
-sensory receives sensations from skin of the cheek, angle of the mouth, deep mucosal branches which pierces the buccinator muscle (but still not motor, they are **proprioceptors**: sensory neurons) and they reach the gingiva of the lower molar region.

Posterior:

-****auricotemporal nerve** is (posterior and sensory). comes from the **upper border** of the **parotid**. sensory neurons from the parotid gland and temporal region close to these branches, external acustic meatus, tympanic membrane, skin of skull and temporomandibular joint. (we saw branches already but they were motor from the masseteric nerve) -no secretion sensory only.

-****lingual nerve:** posterior and sensory, will follow the tongue, part of mandibular division of trigeminal, **doesn't have taste** but the other 4 sensations.
-motor branches don't come from trigeminal.
-will receive one branch of the **facial nerve** so they join together. facial has the **taste** neurons (still sensory neurons though). we get all the senses together cause the **fibers join**. (**point** where they **join** is called the **corda tympani**) -we receive sensation from the **anterior two thirds** of the tongue, **not from the posterior part**. -the branches of the **facial nerve** which has **parasympathetic** innervation will travel together with the sensory branches of the lingual nerve.
-chorda tympani has parasympathethic **branches to submandibular ganglion** and some other glands. but again just sensory.
-we have **motor** nerves that reach the tongue from cranial nerve **X** (**vagus**) ,XII (**hypoglossal**) but not V.
-**anterior two thirds** of **tongue** receives sensations from **V, VII.** taste from facial, rest from trigeminal GSA. apart the anterior two thirds of tongue we have branches of nearby areas: gingiva of lower teeth, sublingual and submandibular glands, isthmus and palatine tonsils. (all of these **sensory only**).
-**posterior third** is from **glossopharyngeal** and other nerves.

****inferior alveolar nerves:** (posterior and sensory) run downward, reach **medial pterygoid muscle** and the **ramus** of the **mandible**. **before** they **enter** the **mandible through** the **mandibular foramen** they **give one sensory nerve** to the **mylohyoid** (which supplies anterior belly of digastric and mylohyoid). (which was motor and posterior, the exception)
there is an **internal mandibular canal** (usually one) through which we receive **innervation to all dental pieces** (one branch only). some patients have multiple branches which join the root of the teeth. (careful with implants placement with them)
-we innervate the mandible bone, periosteum, periodontal ligament, gingiva…

-at the end there are **two terminal branches** at the **level of** the **second premolars**: **mental nerve** and **mandibular incisive** nerve.

-**mental nerve exits through** the **mental foramen** and we are going to give sensory branches to the **chin** and **lower lip**…

-**mandibular incisive nerve** continues **anteriorly** to **innervate** the **canines** and **incisors** which are inferior.

-mental foramen is for the last branch.

-if **wisdom tooth** impacted it could be in contact with branches of the **inferior alveolar nerve**, you need to look at x ray if nerve is compromised or not. **even** the **lingual nerve** could be damaged.

-for a sensory pathway we need three neurons. (1,2,3order)

-first order neuron comes from the area in the head where we receive the sensation.

-synapse **in the nuclei** with the second order neuron, we have three (one in midbrain, one in pons, and the spinal).

-principal pons -> touch

-pain and temperature -> spinal

-proprioception -> mesencephalic.

-second order neuron crosses to the other side to reach thalamus. we synapse in the **ventroposteromedial nucleus of** the **thalamus** with the third order neuron. which then goes to the cortex.

motor pathway we just need two neurons: upper and lower motor neurons. we have one motor nuclei in the trigeminal nerve. the **upper motor neuron** coming from the **cortex** (where the **soma is**) makes a **decision** (e.g to move the masseter).

motor neuron: multipolar, **soma in gray matter and axon in white matter**. **axons** may **cross** or not, **most of** the **times** yes. (when they don't cross they remain on the same side) when they do they **reach** the **trigeminal nucleus** on the other side, **synapse** with **lower motor neuron** which then goes to the muscle.

-motor fibers are **special visceral efferent SVE** and **not** general somatic efferent GSE because the **contraction is not always voluntary**. (what happens with mastication in the supratrigeminal nucleus which is autonomic)

-in the trigeminal ganglion we have the nuclei.

-**proprioceptors send signals** to **many different nuclei** because sometimes we have **involuntary** responses which we call **cranial reflexes**. sometimes we need signals from the propioceptors to **synapse** with **motor nuclei**.

voluntary motor when receives order from cortex

involuntary motor when we receives orders from other neurons (e.g something gets thrown at us and we close our eyes as it approaches)

we also send signals to the limbic system in the brain along with the impulse.

we also send sensory impulses to ganglia which have sympathetic or parasympathetic fibers to regulate secretion.

-everything is connected: **trigeminal-thalamic pathway**. sensory but related to reflexes, emotions, memory/learning.

-unipolar or bipolar -> sensory neurons. GSA fibers from facial nerve synapse in the same nucleus as the trigeminal nerve. this nucleus receives both GSA fibers from trigeminal and GSA fibers from facial. we respond to the two stimuli with the same response. we receive sensations in the same nucleus and we make the same response to different areas. both motor and sensory neurons synapse with other centers (autonomic motor nuclei, emotional brain…)

UNIT 6: Somatosensorial System

sensory neurons: somatosensory system.
no matter if the signal enters spinal cord or brain stem we need 3 neurons for the sensory pathway.
1st order neuron which receives stimulus -> receptor
-sensory neurons are typically unipolar,bipolar **or pseudounipolar** (soma on one side, could be in the way between the dendrite and axon or we could have a very long axon and the soma is on one side). -somas of 1st order sensory neurons are going to be located always **outside** the **cns**. that's why we have a **sensory ganglion**. (e.g. dorsal root ganglion of the spinal nerves).
all the **spinal** nerves are **mixed** and the sensory info enters in the dorsal root where we have the ganglion.
-**motor neurons** are **multipolar** so we don't have motor ganglia (don't exist).
-trigeminal ganglia: where we have somas of the sensory neurons of the three divisions.
-synapses with the 2nd order neuron **either in spinal cord or brain stem**
-2nd order neuron usually crosses to other side and sends signal to the thalamus on the other side of the body. here the 3rd order neuron receives the signal and sends it to the cortex.

-**visceral** receptors: **internal** stimuli
-**external** receptors: detect things happening **outside** the **body**.
-they are receptors specialized in detecting **one type** of **info** and sending it to the cns. (light,taste,smell,touch,proprioception…) -thus they have different specialization and **different sensitivity**. (different threshold for activation).
-**chemoreceptors** inside body (baroreceptors) are **interoceptors**.
-we have both internal and external nociceptors
-there is a difference between sensation (stimulus that reaches cns) and perception (processed meaning from the stimulus). **perception** is **subjective** (depends on person,environment,previous learning/experience..) -sensation is **also** not the same (we don't have the same sensory neurons with the same **sensibility** and **threshold**.)

-modality: vision,hearing,balance..
-sensory neurons: general somatic afferent
(ones of trigeminal: touch,pain,temperature,proprioception),
special visceral -> (neurons that take info from inside: baroreceptors, chemoreceptors..)
special senses: taste,hearing,smell,vision,balance.
-by classifying the fibers you already know what type of info we are getting.

-**touch** receptors. there are many types. (**mechanoreceptors**)
-**dendrites**: area in the neuron where we **receive** the **stimulus**
-**soma**: **cell body where nucleus is**, it is **here** that we **synthesize** the **neurotransmitter** because that's where the **ribosomes are**, we pack them in vescicles and we transport them towards the **axon terminal** where we **store** them. (with the others)
-neurons are excitable cells: capable of receiving a stimulus and responding to it by generating an action potential. there are two types of electrical signals: **graded potential** (**receptor potential**) and the other type is the **action potential**.
-**graded potentials** are generated in the **dendrites** (nerve endings) in response to stimulus
-**membrane** of neurons at rest are **charged** (**not neutral**), because it has a different distribution of positive and negative charges on both sides of the membrane. at rest the **inner side** of the membrane is **negative** with respect to the outside. that's why we say the **resting membrane potential of a neuron is -70mv**. (nothing is happening). -we have active **ion channels** which usually are closed but will open in response to something. -**three types** of **ion channels**: **ligand-gated**, **stretch-gated**, **voltage-gated** channels. they are not everywhere.
-**voltage** gated channels are in the **axon**, **ligand** gated and **stretch** gated are in the **dendrites**. because of this the signals we get are different. we can **generate graded potentials** in the **dendrites** and **action potentials** in the **axon**. different properties as well.
-if we **open** an **ion channel** and **positive charges enter** the **number** will **become** more **positive** than -70 (e.g. -60/ -50..) -> **depolarizing** signal. (cause more positive than -70)

-if **higher** than **-70** (more **negative**) -> **hyperpolarizing**. -graded potentials could be both depolarizing or hyperpolarizing signals. (with different intensities hence the name graded).
-by **stimulus intensity** we refer to **how big** the **difference** is **from** -**70mv**. big difference= high intensity, small difference=little intensity.
-**graded potentials** will **travel** in **all directions**. they will **reach the axon's trigger zone**. (area where we start having **voltage gated channels**, beginning of **action potentials**).
-in **sensory neurons** the **trigger zone is in the first node of ranvier**. (areas in the axon with **high areas** of **voltage gated channels**).
-the axon has myelin
-**action potentials** are **all or nothing** signals (fire or not) because of a **threshold value** of membrane potential in which the **voltage gated sodium channels open**. this value is **-55mv**.
-if we have a graded potential in the dendrite which travels reaching the axon with -55mv or higher we open the voltage gated sodium channels and generate an action potential. the opening causes a very fast **depolarization** of the membrane which **lasts untill** the **channel closes**. **then** we **go back to resting**.
-**frequency**: **number** of **action potentials in time**.

-**light touch**: beginning of stimulus we generate action potentials, we don't generate anymore, then when stimulus disappears we generate them again. (**rapidly adapting**) some sensory neurons work like this.
-in other neurons we generate action potentials all the time, we stop when the stimulus disappears. -we classify receptors according to the way we send the signal.

-the field where the neurons sends dendrites, is not always the same size. (e.g. **pacinian corpuscle** has a **really big receptive field compared with ruffini**). [field where we can receive the stimulus].
-smaller field: detect higher intensity of stimulus.
-when you increase the intensity of the stimulus the response also increases. (**sigmoidal** graph) -> there is a limit of detection for each one of the receptors. we detect a **range**. smaller stimulus we don't react. our threshold of detection for sound in humans is different from the one of dogs. our sensory neurons have a different threshold. this defines our ability to respond to different stimuli.
-**threshold** of detection (e.g pain) is **different** for **each one** of **us**. we also don't see exactly the same colors. -the threshold also **changes during** the **time of** the **day**, and also **depends on our health** etc. (e.g. hyperalgesia-> you react faster to same stimulus)
-threshold: when 50% of the patients respond to the stimulus. (average) lower detectable intensity.
-blind people use touch to get a 3d image of what they are touching, they can do it thanks to the various mechanoreceptors. and each one of those has a limit.
meissner: specialized in thin touch
pacinian: specialized in vibration. detects from **10 to 1000 hz** (this is the **threshold range**) not capable of detecting higher or lower.
-we detect by taking all signals from **all** receptors at the same tipe. they overlap and cover similar areas.
sensory threshold: **minimum amount of stimulus** which is needed for the sensory system to make a response. **minimum detectable unit.**
-**some visceral receptors are somatic**.
-for a sensory neuron to be able to create an action potential it has to generate first a graded potential. a **graded potential** is generated by **opening** the **ion channels**. they are different and open in different ways among receptors. -**specific** for **one type** of **stimulus**.
-mechanoreceptors (pacinian or meissner)

-**ligand-gated channels**: **neurotransmitter binds to ion channel** and the **channel opens**. when we stretch the skin we open the channel -> the area around the receptor changes. **positive charges enter** the **cell creating** a **graded potential**. it **travels in all directions losing intensity**, reaches the **trigger zone** which is the **first node of ranvier**. (if value of -55mv we generate the action potential if lower -> no detection, nothing happens, we don't feel it).

-**action potential travels only in one direction**, **from node of ranvier to node of ranvier and never loses intensity.** -small stimulus will generate small number of action potentials and viceversa, this way we distinguish strong from weak stimuli. -**strong stimulus** can be identified by the **higher frequency** of **action potentials**. -remember we are always in the threshold of detection.

-the signal from the second order neuron can change cause it receives signals from several different receptors (1st order neuron). -they can **integrate info** by **summation. (spatial or temporal)**
-when the action potential reaches the axon terminal we release the neurotransmitters. they **diffuse** in the **synaptic cleft** and **bind to** the **ligand-gated channel of** the **second order neuron in the dendrites**. -in the second order neuron this **causes** a **graded potential**, but **alone it won't reach -55 mv** (to generate an action potential). a few seconds later we receive another signal from another neuron. if the **neurons are close in space** they experience **spatial summation**. (we generate action potential because we reach -55mv). thus depends on **how many receptors generate** the **signal** and whether they are **close or not**. (time and space)

-the neurotransmitters in the synaptic cleft get recycled, there are enzymes and mechanisms to remove it.
-if the **neurotransmitter** is **released very fast** (before the nt of the previous action potential disappears we release more) we **may still reach -55mv**. -> **temporal summation**.

-**adaptation**: sensory **receptor** cell becomes **less responsive** to the **same** (**unchanged**) **stimulus**. -has to do with **1st order neuron,** sending less signals to the second order neuron.
-**habituation**: sensory **receptor continues sending signals** but you have the **stimulus all the time** so you **stop processing it in the 2nd order neuron**. (**ring of marriage** you stop feeling, the stimulus is still there, the neurons know but the brain stops processing it. even with your **clothes** when you wear them all day.) -when you remove the stimulus you realize/feel it very strongly.

-some receptors generate **action potentials** at the **beginning of** the **stimulus**. the **stimulus** is **persistent** and we don't do anything until the **stimulus disappears** and we send **action potentials again**. **typical to touch receptors**. they **detect change**. classified as **rapidly adapting receptors**. **no change -> no action potential.**

-other receptors send **signals** at the **beginning** of the **stimulus** and **as long as** the **stimulus** is there they **continue doing so**. until the stimulus disappears. typical of **nociceptors**. -> **slowly adapting receptors.**

-**not all receptors in the body can have habituation**, we can have it with touch receptors because we need it. but for example **baroreceptors** (which are also sensory neurons) which need to detect blood pressure **all the time** can't experience it. -> **maladaptive** receptors. these are the ones **necessary for life**, we need their info all the time. (chemoreceptors, baroreceptors…) they are **tonic** receptors, they are the limit of the slowly adapting if you have to classify them.

-we can have the opposite of adaptation -> **sensitization**. in this case we **repeat** the **same stimulus but** the **response** is **higher**. common with **pain**. (you had pain in a region for a long time, when you simply touch it, it will hurt, the area is sensitized.)

-with **adaptation** and **habituation** there is **no motor response**. with **sensitization** instead there is a **higher motor response**.

-**pacinian corpuscle** for **vibration**: if you **active** it we get a **response**, if you **keep doing** it there is **no response**, but when you **remove it** there is an **action potential**.
detects changes in stimulus. -> **rapidly adapting receptor**.
not sending signal (action potential) all the time, just when there is a change. **action potentials** in the **beginning and** in the **end**. sends signal when pressure is released. while the stimulus is

there,there is no signal. **if you increase the intensity you will have action potentials though**. it's the receptor with the **fastest adaptation**.

-**slowly adapting** receptors: as long as stimulus is there the send the signal. **tonic**.
-we have combination of rapidly and slowly adapting receptors, so you are feeling things all the time which you might be habituated to but you also feel the change. each one of them have a different threshold, even if they belong to the same group. **muscle spindle (proprioceptors) are tonic**. you know all the time your position in space.
-slowly adapting receptors may undergo **accomodation** (**eye**) -> able to focus far away objects even at rest.

two point discrimination: ability to **discriminate two points** as two points when they are **really close** to each other. has to do with the **receptive field**.
receptive field: area that receives signals and gives them to a sensory receptor.

-if receptive field is big the moment the neuron gets excited the whole field gets activated, and so does the nearby field -> **big field**: **less precise sense**.

-for two point discrimination we **need** a **small field** (e.g. **retina**, field for each sensory neuron [1st order, receptor] is **really small**, that's why the **sharpness** and **contrast** of the pictures we actually see is this good). if the **field** was **bigger** we would have a **more blurry** image.
smaller field -> greater sensitivity, bigger resolution.

-we can feel touch in all the areas in our skin, but we don't have the same feeling in all the areas. there are **areas where we feel** it **better** (e.g. **tips** of **fingers** and **lips**). when you have someone write on your back it's hard to understand what they are writing cause the field is bigger. **sensory field is smaller in the tips of fingers**. for different senses we have different sensory fields.
-there is a field for the second order neuron too (determines how many neurons send the signal to it, and it is where we can experience temporal and spatial summation). sensation depends on the signal from the 1st order neuron (receptor) and how many receptors are sending signals to the second order neuron.

-lateral inhibition: many sensory systems have **very small fields** (e.g. the **eyes**), having a very **good two point discrimination**. that means also that my **first order sensory neurons** are **very close to each other**. so if you **focus** your **attention** in **one of them** there are **inhibitory interneurons** from the particular place you're focusing the attention to which **inhibit** the **synapse of the lateral ones**. we do this to **increase** the **contrast** of whatever is calling my attention. happens a lot (e.g. someone calls your attention in the bar, you see that person and no one else). it is a **physiological response**. happens **also for touch**. collateral inhibition -> focus on one side, lose the sight of the other two.
-**axon collateral**: branch of the main axon. lateral inhibition happens because sensory neurons send axon collaterals to the nearby neurons, **inhibiting them (by themselves or through an inhibitory neuron).**

UNIT 7: Types of Sensory Receptors

-most of sensory neurons are on the surface of the skin.
-first layer of skin: epidermis -> keratinized stratified squamous epithelium. **epidermis is not irrigated but innervated.**
-the nerve endings of some neurons reach the epidermis, which allow us to feel the stimuli.
-**nociceptors**' **free nerve endings** reach the skin's **epidermis**, that's why we feel pain really early.
-**dermis**: **connective tissue**. both **irrigated and innervated**. **high density of mechanoreceptors** here. some of them reach the epidermis but not all of them.
-there are more superficial and deeper receptors. some of them are close to the **hypodermis** where we have **adipose tissue** and **areolar connective tissue**. hypodermis is also **irrigated** and **innervated**. some **mechanoreceptors**, such as the ones for **strong pressure** lie close to the hypodermis or in it.

-**light touch**: the receptors will be **superficial**.
-**crude touch**: pressure has to be high, we are activating **deeper receptors**.
-all this info **reaches** the **somatosensory cortex** in the brain and we **process** it.
-somatosensory are **GSA** fibers: touch, proprioception, pain, temperature. the other neurons are special senses. (taste, light, smell)
-touch: receptors for **fine** (**superficial** mechanoreceptors) and **crude** (**deeper** mechanoreceptors) touch. fine touch can recognize the **size, texture, shape, smooth vs rough, moving or not**…
crude touch: we know that something is touching and creating pressure but we don't discriminate fine perception.
-**vibration** belongs to the touch perception. -**pacinian** and **meissner** corpuscles receive **frequencies** of **vibrations**.
-**sweat** and **sebaceous** glands are found in the skin. they respond to **sympathetic innervation**. so next to these sensory receptors in the skin (mechanoreceptors) we can find sympathetic fibers. they are not specialized in sensing but in increasing or decreasing secretion of the nearby glands. anyhow the two **neurons** run together **in the dermis**.
-**sympathetic motor fibers** target: **sweat glands** in skin, **vascular smooth muscle** of the blood vessels (vasoconstriction or vasodilation), the **rector pili muscle** (**contraction** of **hair** is **involuntary**, depends on autonomic nervous system -> sns, pns.) and other glands.
-**there is no parasympathetic innervation of the skin**.

-we can find **sensory neurons** of **two types**: **A** or **C**. (**general classification**)
-**c fibers do not have myelin** and are **very thin**.
-**a fibers** are **myelinated**. variety of a fibers (**4 types** but all have myelin).

-the dendrite is where we receive the stimulus which can be depolarizing or hyperpolarizing. travels and reaches the trigger zone (place where we decide whether to trigger or not an action potential) which is found in the first node of ranvier. if the stimulus is depolarizing and reaches the threshold value of -55mv then and only then the action potential is fired and only travels in one direction (from the trigger zone to the axon terminal). upon reaching the axon terminal the neurotransmitter is released. this process is common for every sensory receptor.

-**amount** of **myelin differs among receptors**. myelin is related to the **speed** of **conduction** of the **action potential**. the **wider** the **axon** the **faster** the **conduction**. **(cause less resistance).** the myelin going around the axon increases it's diameter. this means the signal will always be much faster in the A fibers than in the C fibers.
-**c** fibers conduction velocity: **0.5 - 2 m/s**.
-**a** fibers conduction velocity: **6 - 120 m/s.**
-another difference between receptors is the area covered by the dendrites (how many dendrites we have, are they covered by capsule or are they free) this info will tells us how sensitive the receptors are (how much it will recognize and in what frequency). this also gives us an idea of the sensory field (area of the skin where you receive dendrites of the neurons).

-a fibers can be **a-alpha (α) a-beta (β) a-gamma (γ) a-delta (δ)**
-can also be classified into: **I (Ia or Ib), II, III, IV.**
-**c-fibers are the IV.**

-**c-fibers** detect: **crude touch** and **pressure**, **tickle**, **aching pain**, **cold** and **warmth**. these are the types of sensory neurons. **no myelin** -> **low conduction velocity**. we feel aching pain even if they are slow because they are **very sensitive** to the stimulus, really good in recognizing (sensing) pain. (they are **superficial**).

-**a fibers have myelin**, **faster**, recognize different types of stimuli and they are **not going to be so superficial**. we can find them in other regions. (**pacinian corpuscle** (**a-β** for **vibration** is the **deepest** of the **mechanoreceptors**).
-**hair receptors belong to several groups** (**a-β and a-γ (gamma)** so it has properties of the two of them. in the other **classification** it belongs to **I,II, III.**)

-anesthesia just blocks pain and not all the time. you don't necessarily want to block all the fibers. each one of the agents used for anesthesia is capable of blocking different fibers. sometimes you just block pain and not touch. (patient doesn't feel pain but he can feel his touch/pressure in that area). in this case you just blocked the pain fibers and not the pacinian corpuscle. **the anesthetizing agent will reach more easily the unmyelinated c-fibers than the myelinated a-fibers**.

-second classification made by physiologist specialist for sensory perception.
groups I,II,III,IV. IV is C. I,II,III is A. I has Ia and Ib.
group IV-> **C**: thin, **0.5 - 2 micrometers diameter**
I,II,III -> differ in amount of myelin.
Ia is the fastest. III is the slowest. **Ia the one with the most myelin**. myelin covering with different widths.
-**muscle spindle** and **golgi tendon organ** are **tonic receptors**, they send signals all the time as long as the stimulus is there -> **slowly adapting**. a **lot of myelin** cause all the time sending the signals, they **need to be fast**.
-**deep pressure** and **touch** -> **pacinian**. send signal at beginning and at the end. detect change. -> **rapidly adapting**. (when you touch and stop touching). they **don't need to be so fast**.

group Ia -> muscle spindle *17 microns in diameter*, **fastest** and **thickest**. **A-alpha**. **tonic**.
group Ib -> golgi tendon. very **similar**. *16 micrometers in diatemeter*. **A-alpha**. **tonic**.
group II-> fibers from cutaneous touch receptors. *8 micrometers in diameter,* speed of conduction a bit slower than the previous ones. **A-alpha or A-beta**.
group III -> closer to group IV characteristic-wise. 3 micrometers**. A-delta** fibers. for **temperature, crude touch, pricking pain.**

-if we have a **free nerve ending** in the **dendrites** it's usually a **type c** fiber. **pain**, **temperature**, **unmyelinated but** the nerve endings **reach** the **epidermis** and they are **really sensitive**.

-sometimes the **nerve endings** have a **protection** and are **covered** with a **membrane or layers** of **connective tissue**. -> **encapsulated nerve terminals**, they are in the **dermis**.
-there are also specialized receptors

-**epicritic vs protopathic** sensations.
protopathic -> **primitive** sensations: **pain, temperature, pickles**. they pass through **free nerve endings** and **c fibers** usually.
epicritic -> **judgement**, we **discriminate**. **fine aspects** of **touch**, **receptors with** the **capsules** are the **mechanoceptors** for **touch**. **a fibers**. gives **topognosis** (recognizing the 3d shape of something which is touching us). **vibration** also included in this modality. (**meissner** and **pacinian**)

-**two point discrimination** -> details. not the same everywhere, there are **specialized areas** such as the **tips** of **fingers** and **lips**. *small field and more detail and stereognosis*.

-mechanoreceptors for touch, vibration and proprioception.
-thermoreceptors for temperature
-**chemoreceptors** are **interoceptors** (oxygen and co2 -> chemoreceptors in the carotid arteries and arch of the aorta) **osmolarity** (adh -> vasopressin, hormone responsible for thirst, related to the reabsorption of water in the kidney.) we **receive** the **signal** (change in osmolarity -> chemoreceptor) in the **supraortic nucleus**. there are also **chemoreceptors** for the amount of glucose, amino acids, fatty acids. we reach and send the **signal to** the **hypothalamus**, if there is low glucose we secrete insulin…
-one of the chemoreceptors is a specialized sense fiber: (**taste**,**smell** -> specialized afferent fibers **SVA**)
proprioceptors: send info of position and balance. (present in the skeletal **muscle**, **joints**, **tendons**, **inner ear** [vestibulocochlear nerve])

-**mechanoreceptors**: for **touch,pressure,vibration and proprioception**. located in the skin with other cutaneous receptors. A-beta fibers with the exception of the ones with free nerve endings which are a-delta, they are more similar to c fibers. nociceptors and thermoreceptors are not included. (cause those are type c fibers).
they can be slowly or rapidly adapting receptors. some of them are in skin with hair and some just in hairless (glabrous) skin. e.g tips of fingers.
-if the skin has hair the hair is always associated to a nerve plexus, a sensory neuron. we will receive sensation there -> hair receptor. if there is no hair we need something similar -> **meissner in glabrous**.
-the limit between epidermis and dermis is never a straight horizontal line. it goes up and down generating epidermal bridges and dermal papilla. dermal papilla are needed for the receptors to reach the epidermis.
-meissner is located in the dermis but it is really close to the epidermis so we need to make room for it, which is why we make the dermal papilla and the epidermal bridges.
-sensory neurons need oxygen and nutrients -> need blood vessels. there are two networks of blood vessels in the skin: one is the superficial vascular network and it's found in the dermal papilla. the other one is the deep vascular network. both the hair and the receptors receive blood supply.
-the top of the skin without hair is not flat either. we have circular patterns folds of the epidermis (not the same as epidermal ridges), responsible for the finger prints.
epidermal ridges: projection of epidermis towards dermis.
circular patterns: projections towards the outside.
-glabrous skin has a very dense matrix of mechanoreceptors. the feeling of touch is better in the regions with no skin. (lips and finger tips)
-mechanoreceptors don't include nociceptors and thermoreceptors. they detect vibration and touch in different modalities.
if free nerve endings -> a delta fibers. receptive field may be big or small. aching pain is C. we reach the epidermis, while in all the others we stay in the dermis. somatosensory refers to a delta not c. but both of them have free nerve endings and reach the epidermis. c fibers do not have myelin and a fibers do.
thermoreceptors and nociceptors (some of them are a delta) also have free nerve endings. a beta don't have free nerve endings while a delta do.
vibration is found in meissner, pacinian and krause bulbs.
pacinian and ruffini have large receptive fields the rest have a pretty large.
fastest speed of conduction is the pacinian. (phasic: sends signal at beginning and end).

meissner: long mechanoreceptor for touch, **a beta**. no free nerve endings.(stay in the dermis: **dermal papilla** in the **skin** without hair ->**glabrous**) there is something to cover the dendrite: specialized in receiving one modality. it's specialized in **discriminating touch**. can detect vibration but in a very small frequency. rapid adaptive and small receptive filed cause it is for fine touch. there is a single dendrite within a corpuscle that acts as a specialized structure. coupled mechanically to the edge of the papillary ridge. (occupying most of the space). the structure covering the free nerve ending is supporting squamous cells with a connective tissue capsule. a single nerve fibers reaches inside. vertical orientation with respect to the top layer of the epidermis. at the beginning we have one to six axons entering the corpuscle and then they ramify in just one branch terminating in connective tissue layers (lamellae) that are making the capsule around the receptor. the lamellae have also been seen in the bone tissue but this time it's connective tissue. similar to an onion.

epithelial tissue: a lot of cells with no space between them.
epidermis is always touched to a basement membrane (basal lamina). and underlying it is connective tissue: dermal papilla.
-meissner and merkel are the two most superficial.

merkel disk: made by two cell types -> one is an epidermal cell in the epidermis and the other one is a neuron. (always painted yellow). nerve ending of neurons gets in contact with epidermal cell which is always located in the **stratum basale**. (in contact with the basal lamina). in this layer we find keratinocytes and melanocytes, and merkel cells. not classified as free nerve ending cause it has the merkel cell on the top. **a beta** fibers. receptors for **gentle touch**, superficial. slow adaptation, tonic response -> sending signal all the time. small receptive field cause they are for

thin touch. usually found in the center of the papillary bridge. in between two meissner corpuscle (which are found in two dermal papilla). on one side you have a meissner then you reach the top and have a merkel and then another meissner. **can be found in both skin with and without hair**. even mucosa and superficial layers, everywhere. if we have hair we group them in specialized structures called hair disk. a beta fibers have branches that could reach 90 different areas. each one of the nerve endings has one merkel cell.

lamellar corpuscles: pacini. lamellar: layers of **connective tissue**. (fibroblasts and collagen are found too). subcutaneous in hands and feet. it is deep, really close to the hypodermis. not for thin touch, it's for **vibration and high pressure**. large receptive field. high frequency of vibration. there is a capsule covering the endings. dendrite is covered by different cells, sometimes making myelin, and then a capsule of connective tissue. light pressure won't reach the dendrite. in order for the stimulus to reach the dendrite we have to make a deformation in this area (this includes a high pressure). good for vibration cause when we have a high frequency of vibration the connective tissue will vibrate reaching the dendrite.
-all receptors for vibration have a capsule for connective tissue and when the capsule vibrates the stimulus is felt in the sensory neuron. **most a beta but some can be a alpha** cause they are a little faster. pacinian corpuscle is the **fastest** of all the **mechanoreceptors**. we have a capsule and then a central space where we have the terminal (dendrite).

ruffini: in the *middle, not in the surface and not the deepest*, it's in between. found in **both skin with** and **without hair** like merkel. elongated spindle (multiple branches that don't go in a horizontal line). it is encapsulated, covered by collagen and a capsule of connective tissue. not a free nerve ending. a beta fiber, some of them are faster -> a alpha. they are not as fine as merkel and not as crude as pacinian: for tissue **stretching**, **pressure** (not as much as pacinian).
they are **tonic -> slowly adapting**. we feel movement of finger tips, shape of objects… we also have them in ligaments and tendons because they have structures similar to the muscle spindle.

hair terminal organs: hair is made by keratin, needs to enter the dermis. (where we have the hair matrix -> we encounter the cells that are dividing and generating the keratinocytes that make the hair). all this area in the dermis has blood vessels and is innervated. each one of our hair is surrounded by one sensory neuron. when you touch the hair the movement is felt in the neuron that is around the hair root; this send the signal that is necessary to feel fine touch. not as precise as the others, it's **diffuse touch**. it's a **rapidly adapting** receptor. f**astest after pacinia**n. of course only found in skin with hair. if we could classify it, it is really similar to the free nerve endings, cause there is no capsule/connective tissue around the dendrite. **a type fiber** but with structure of free nerve ending even though it **doesn't reach the epidermis** but just the dermis.

discrimination between two points: ability to differentiate two really close points and identify them as separate. you can do this when you have a really small sensory field. the smaller the better the discrimination between the two points. (sensory field big -> you see a lot of pixels and can't discriminate; while sensory field small -> a lot of nerve endings reaching the area and we discriminate much better). fingers have a very good two point discrimination (allows blind people to read braille by touching). some other areas are not so good such as the back. (discrimination small cause sensory field much bigger).
dermatome: field of the skin that receives innervation from the same nerve.
all the sensory neurons enter the spinal cord through the dorsal root ganglion. (accumulation of somas of neurons outside the cns). if the receptor is found anywhere from the neck or superior then we synapse with the second order neuron. with the brain stem directly. (e.g. trigeminal nerve -> synapse with the nuclei which could be in the midbrain/pons/spinal).

with epidural anesthesia which is done in lumbar region you only anesthetize the legs because that is the dermatome. if you touch your leg you don't feel it but any other area of the body yes. careful because when you anesthetize one region the others are still working and feeling.

the five fingers have different two point discrimination (thus different concentrations of mechanoreceptors). same thing for the areas in the hand.

merkel we have them everywhere, but not in the same amount. the tips have much more. (cause it's for fine/discriminating touch). same thing for meissner. these two are the ones found next to each other.
ruffini (one in the middle), which is not needed for fine and discriminating touch doesn't need to be found in high concentration in the tips of the fingers. there is a general concentration everywhere.
pacini: everywhere, but a little bit more in the finger tips even if not specialized in discriminative touch (thus not such a higher density).
when you touch an area you are activating several receptors at the same time, the information is coming from different ones. we integrate the info of all of them. we discriminate what we are touching depending on the comparison that your cns makes b/w the different sensation which it's receiving. if the area is very small the sensory neurons will send more action potentials. (thus more precise). thus, when something is very thin, we are activating a lot of meissner and merkel cells and they are generating many action potentials.
-cns sees from what neuron it's receiving the sensation and how many times is the signal arriving. processing this info gives such a good sense of touch.
-for braille the spacing between the points has to be within the threshold that humans can detect. there is a spacing field that we can detect. we need to train for this. (we have a receptive field diameter which could be acquired or different between people with training)

-nucleus: accumulation of somas of neurons in the cns. in the gray matter. (e.g. spinal (for pain and temperature) and principal nucleus of trigeminal (for touch). signal from first order neuron reaches the nucleus and synapses with second order neuron which goes to the ventro posteromedial nucleus in the thalamus. it is here that we synapse with the third order neuron which then goes to the cortex. (different areas of the cortex).
from the thalamus we don't just make a single synapse, we can send the signal to many different areas. we send the signal to multiple areas in the cortex (as we receive different stimuli all at once such as pain, temperature and touch). the two signals travel together as they reach the thalamus but then they are sent to different parts of the somatosensory cortex (where we have regions that are specialized for different sensations). -thus, even though the original signal could be felt as something really small we are really activating a lot of areas in the brain, and at the same time. (integration process -> receive many signals, process all of them and send them to the appropriate areas in the cortex, we make sense and decision from them.)
-some neurons are going to reach some regions in the cortex and some other will synapse with axon collaterals and dendrites.
-depending on the type of third order neuron that receives the signal sometimes we could be activating 3 or just 1 fields. at the end what matters is the area of the cortical cortex that we are activating when we receive the sensation. this is always the somatosensory cortex.
-map of the cerebral cortex: each area of the gyrus would be receiving a different sensation.
the receptor fields that we have in the cortex are different. (area in the cerebral cortex with a field for one type of sensation, not the same as a dermatome cause that's an area of the skin that receives dendrites from one sensory receptor of the 1st order neuron).
-the cortical receptor field is the area in the cerebral cortex where the third order neuron sends the information. -larger than those in the skin (when you touch something with your finger the sensory field of the dermatome in the skin has a size; but when you reach the cortex, the area that receives that sensation is bigger, because the third order neuron is huge and synapses with other neurons. and we also have the interneurons and they process the information).
-the cortical field for sensation is larger than the receptive field in the skin.
-areas where we receive a lot of sensations are larger.
-gyrus: big sulcus in the brain. if it is small -> folds.
-there is a really big somatesensory gyrus. (post processing areas are the largest receptor fields)
-hotspot: where we receive a lot of information.
-plasticity: not fixed, subject to variation.

-trigeminal nerve is mixed because it also has a motor division which is the mandibular. this division has SVE fibers (special visceral efferent).
-GSA fibers (general somatic afferent for the 4 sensations of the somatosensorial system). we need three neurons. either unipolar or bipolar. (long axon, soma on one side, and have a dendrite). nerve ending where we feel the stimulus. they can be unmyelinated fibers C or myelinated A (4

groups depending on amount of myelin: from most to least -> alpha, beta, gamma, delta). this is just for the first order neuron -> the receptor.
-there are 5 mechanoreceptors (meissner, pacini, merkel, hair root plexus, ruffini).
-mechanoreceptors are a beta fibers with the exception of the hair root plexus which are a delta.
-classified in two groups -> type 1: closer to the epidermis and type 2: deeper in the dermis. classification is because we have fine and discriminating vs crude touch.
fine touch: (know the size, shape, texture) discriminative. we have the type 1, they are superficial so we can feel the sensation quicker. for crude touch instead we have pacini and ruffini. (type 2).
-we also have different amounts of receptors, glabrous skin is highly specialized in fine touch (tips of fingers and lips). thus glabrous skin is very rich in type 1 mechanoreceptors, (meissner,merkel) found in high concentrations and with small receptive fields.
-to process the information we need to distinguish the type 1 with the type 2. one of the ways to do it is to have a slowly vs a rapid adapting receptor. when you look at the two type 1 (meissner and merkel) one is a rapid adapting and one is a slowly adapting. the same happens with pacinian corpuscles and ruffini. (deep type 2 receptors)
-when the stimulus is small so is the number of action potentials.
-v1,v2,v3 have somatosensory receptors which are all collected by the mandibular division (v3).
-if you block the mandibular division with anesthesia you will still feel the nose. because different dermatome.
-the 4 types of somatosensory receptors (1st order neurons) of the trigeminal nerve send the information to the 2nd order neurons present in the 3 sensory nuclei. (midbrain -> mesencephalic for proprioception, pons -> principal for touch, pons to spinal cord -> spinal nucleus for pain and temperature) there is 1 motor. each one of them has it's own nucleus, but since when you feel something you activate them all you can see with the electrode that they all activate (when something touches your face you also feel it's temperature).
-the second order neuron reaches the ventroposteromedial region (VPM) of the thalamus if it's coming from the head, ventro posterolateral (VPL) if it's coming from the rest of the body.
-if you compare the area which is activated in the somatosensory cortex with the area in the nucleus where we receive the information, the area of the cortex will always be larger. cause in the nucleus there is just the stimulus but in the cortex we are processing (understanding the meaning) of the stimulus so we need interneurons. (more complex) -interneurons make synapses with many other neurons because when you touch something you can be sending the signal to many different parts of the brain. (something pleasant -> we elaborate a thought and a memory, we don't just stay in the primary somatosensory cortex (just for the signals of the receptors, not involved in memory). if we want to remember something that I felt I have to send this to the neuron responsible for **memory** (found in the **lower hypocampus**).
-conscious decisions to remove the hand for example also don't happen in the somatosensory cortex cause it's not a motor area.
-when you look at the surface of the brain it's not flat -> has grooves and folds. name for the groove if small -> sulcus, if big -> fissure. fold -> aka gyrus.
-all spinal nerves are mixed that means that we have both sensory and motor neurons. but these enter and leave the spinal cord in a different position. -spinal nerves have two roots (one is anterior-ventral and one posterior-dorsal). when the nerve is going to enter and leave the spinal cord the neurons are going to localize in one of the two roots. -the **sensory neuron** enters the spinal cord through the **posterior root**. this is why we have a dorsal ganglion. sometimes we stay here if there is a reflex but most of the time we send information to the brain. in order to do that we need an axon with myelin (white matter). going up to the brain I need to use a tract.
-there are 3 tracts in the spinal cord (posterior, lateral, anterior). in case of the sensory neuron the nearby tract will be used -> posterior column pathway tract (most common sensory pathway). some info also goes laterally and very few anterior.
-cerebral hemispheres are studied in lobes because some of the sulci are a little deeper, and this allows to differentiate 4 lobes, which have the same names as the bones (frontal, parietal, temporal and occipital).
-in the brain there is a sulcus in the center which is called central sulcus. this separates the frontal from the parietal lobes. it is where the sensory info arrives. the central sulcus defines two gyri -> a pre-central (anterior gyrus) and a post-central gyrus. this is a primary area (where a lot of information starts).
-sensory information travels posteriorly so it will reach the posterior sulcus **post-central gyrus**. this is why in the post-central gyrus we find the **primary somatosensory area/cortex**.

-the anterior root of the nerve in the spinal cord is motor. most descending pathways are thus anterior -> anterior pre central gyrus. (where most of the motor info is coming from) -> primary motor area.
-primary somatosensory area and primary motor area are side by side so that the synapse is close. (we need easy communication between them. e.g. I touch something and decide I want to take my hand away -> we need synapse with the primary motor area).
the primary somatosensory area and the primary motor area are two parallel gyrus, one of them belonging to the frontal lobe (motor) and one to the parietal (somatosensory).
-if you take a section of the brain you find the gray matter [somas,dendrites,axon terminals, stuff with no myelin] peripherally (outside) and the white matter inside. [axons with myelin].
-the third order neuron which goes from the thalamus to the cortex is not sensory, it's a normal multipolar neuron. (the soma is in the thalamus because the thalamus is gray matter). the axon (white matter) will reach the cortex and the axon terminal of the third order neuron is in the primary somatosensory cortex.
1st order neuron: receptor, unipolar or bipolar. synapses in the nucleus if trigeminal nerve (gray matter) or if spinal nerve synapses in the spinal cord.
2nd order neuron: not sensory, multipolar [one soma in the gray matter of the cns, many dendrites, one axon which crosses to the other side] (soma in the nuclei, axon terminal goes to the thalamus)
3rd order neuron: multipolar, soma in the thalamus, axon from white matter goes from thalamus to cortex.
-they all belong to sensory pathways but just the 1st order neuron (receptor) is sensory, the others belong to an sensory ascending pathway but you don't consider them as sensory. (not sensing, just receiving). they have a different shape, send the signals to other areas in the cns.
-in the gray matter we find the axon terminal of the third order neuron, and now we are going to synapse with other neurons in the gray matter. (not sensory nor motor, they are interneurons).
-interneurons make connections with many order neurons and this why when the sensation reaches the primary somatosensory cortex we can send signals to many other places depending on what we need.
-the primary somatosensory cortex has sub areas (smaller). **[1,2,3a,3b] -> 4 broadman's area**. (area which receive and process only one type of information). 5 belongs to another gyrus not the primary somatosensory area. -they are not in the right sequence, they are ordered in the way broadman studied them. (3a,3b,1,2 from most anterior to most posterior)
-we send information to all areas, but **most of the somatosensory info goes to 3. (either 3a or 3b)**. [mainly proprioception and touch which come from different nuclei (principal-touch) (mesencephalic-proprioception)]. we separate them -> **proprioception** goes <u>mainly</u> to **3a**. (not exclusive). **touch** (most of mechanoreceptors) go to **3b**. some of the info is also sent to 1 and 2.
-at the end we make a combination of all the areas and that's why the sense of touch is so good. (many neurons are being activated at the same time).
-when you're sending a signal to 3b (touch) you also send it to 1 usually (where we process the info: size, shape, texture [more accurate tuning of the signal coming from the other area].
-when you send it to 3a (proprioception) you also send it to 2. (because 2 also receives signals for the coordination of fingers for which we need to know their position)
not exclusive, and anyway most of the info goes to 3 first.
-we synapse with **interneurons** which send the signal to other areas, when you want to process information further to feel something better, they **send the info from 3 to 1 and 2**. -> process known as **fine tuning**. (e.g. searching for keys in a purse without looking inside, you have both car and house keys, so we need to touch better. we send most of the information of touch to area 3 but I am doing fine tuning, also sending info to 1 and 2. when you want to know really well what you're touching).
-even though 3a and 3b have independent proprioceptions, both of them send signals to 1 and 2 at the end. we can send info to other areas which do not belong to the primary somatosensory area by making different synapses.
interneurons: have the soma (shaped like a triangle) and many dendrites and one axon going down or laterally. organized in regions of the cortex.
-in the third order neuron it is the axon terminal that reaches the cortex. the third order neuron has two axon collaterals (branches of the axon). it's actually sending the signal to two other neurons. we make connections with interneurons nearby and going down, multiplying the possibilities.
-we receive the info in the primary somatosensory area, but from there we can go anywhere. (limbic system, hypocampus etc.) any other nearby neuron.

-all the info coming from the feet reaches a specific region of the primary somatosensory cortex. and so is for all the other body parts, they don't all go in the same place, they are organized. (regional organization of the areas of the skin). the areas also have different sizes (e.g. the area of the lips is bigger than the one for the eyes, which have less mechanoreceptors and a smaller area in the cortex for receiving info). feet also have a very big area and a lot of somatosensory receptors (that's why tickles you feel a lot). -remember the area in the primary somatosensory cortex is larger than the area in the skin where you actually feel the sensation. (cause you need to process this info and make all of the synapses).
-areas where we process the information (1 and 2) are bigger than areas 3a and 3b.
-one receptor field from area 3b might make synapses with 400 different neurons. (a lot of info/ synapses at the same time -> hotspot). -the signal has two properties: elasticity and discrimination by lateral inhibition. since the neurons are lateral to each other if you concentrate on one of them you inhibit the ones on the side.
3b and 1 -> fine touch.
3a and 2 -> proprioception
-the brain has organized information to receive info from each sensory neuron (1st order) only in one region of the cortex. all the receptor fields of one skin area send signal to the same column in the same broadman's area. the column which is receiving info from only one skin area is also organized. (because different receptors, each one of them has it's own room).
e.g fine touch -> merkel disk and meissner corpuscle, [both of them a beta fibers, but one is rapidly adating and one is slowly adapting] we don't want to get the signal of both mixed so the receptor modalities have each their own place in the same column. (organized and not mixed)
-we feel something, it goes to it's right place in the cortex, it can be forwarded by the interneuron, but it gets processed in the primary somatosensory cortex in a <u>specific</u> broadman area. (e.g. there is a specific region for the hand) in the column you have different modalities.
-we are sending signals from the primary somatosensory area to the primary motor area back and forth in a coordinated way. (thanks to interneurons).
-from the primary somatosensory cortex you can go more posterior -> posterior parietal lobe (sensory) for integration.
-or you can reach the secondary somatosensory cortex, from which you can go anywhere (anterior parietal lobe and frontal lobe -> motor area to coordinate movement with sensations)
-if you send info to a motor cortex it's always voluntary. if not it's a reflex.
-we also have descending pathways that go to the thalamus, brain stem and spinal cord (for reflexes).
-when you want to learn you need to send the signal the areas in the brain specialized for memory and learning. or if related to emotions -> limbic system. (where you elaborate a thought/link it to an emotion.)
-we reach the primary somatosensory area first and then the other areas.

-**<u>proprioceptors</u>**: receptor for position. found in the skeletal muscles.
there are two types: muscle spindle and golgi tendon organs.
-we want the signal to be fast (if I'm going to fall I need to respond fast to this -> **a alpha** fibers)
muscle spindle mostly a alpha, but might have some a beta and a gamma.
golgi tendon are a **gamma**. both have myelin so still really fast signal.
tonic receptors: signal all the time as long as the stimulus is there. **slowly adapting** receptors.
they differ in fiber and location. muscle spindle: found in the middle of the muscle
golgi tendon organ: found in **tendons**.
tendon: dense regular connective tissue used to attach the muscles to the bone.
the proprioceptors are in the middle of the muscle and in the tendons.
we have two different locations because when you stretch a muscle the muscle is not regular all the time. (e.g. the quadriceps which can be stretched in many directions/sides).
muscle is made of skeletal muscle fiber. a muscle fiber is a single cell. they are multinucleated and the cytoplasm is full with actin and myosin grouped in sarcomeres which contract. all the fibers in the muscle are parallel to each other and go in the same direction. the size is different though -> the skeletal fibers in the middle of the muscle are a little thinner than the others.
-they receive sensory neurons, and their dendrites wrap around the muscle fibers in the middle -> hence the name muscle spindle (wraps around the muscle fiber). the dendrites are protected by a capsule of connective tissue. -> fibroblasts. all the muscle fibers have connective tissue around (endomysium). the neuron enters and the dendrites go around. the dendrites have to be able to sense the stimulus -> need an ion channel to generate graded potentials. (3 types: voltage gated,

ligand gated, stretch gated) they have **stretch gated ion channels**. when relaxed nothing happens, when contracts the stretch actives the stretch gated ion channels in the membrane of the dendrites of the sensory neuron -> generate an action potential and we feel it. (respond to stretching). -they give info about position (positional sensitivity -> standing but still feeling) and movement (dynamic sensitivity).
-both sensory neurons going around a muscle with a capsule of connective tissue.

-passive stretching: no voluntary decision to contract the muscle. the activated sensorial neuron connects **directly** with the motor neuron inducing muscle contraction.
[e.g. quadriceps femoris -> muscle in the thigh. attached to the tibia through a ligament that goes over the patella (on the knee). [patellar ligament] and then we have the tendons which are lateral. if you apply pressure on the ligament you're pulling it down, stretching the muscle (passive stretching, didn't do it consciously). muscle spindle in the quadriceps is going to be stretched and activated and sends the signal to the spinal cord, which is cns. here, without needing to send the info the brain we are going to respond immediately (reflex). cns understands that stretching of muscle means falling because I didn't do it voluntarily so by response contracts immediately. (motor neuron goes to the muscle and make it contract).]

-golgi tendon: you have one muscle responsible for flexion and the other one for extension. (perform opposite movements). muscle that makes the movement -> agonist. opposite movement -> antagonist.
-in these muscles we activate the contraction of the agonists and we inhibit the contraction of the antagonists. (reflex)
-propioceptors also send the signal to the **cerebellum** -> organ responsible for balance and equilibrium, not only the primary somatosensory area.

UNIT 8:

both thermoreceptors and nociceptors or unipolar or bipolar neurons with **free nerve endings**. (no capsule of connective tissue).
-they are going to be either **c fibers or a delta**.
-most of them will be in the epidermis as they are free nerve endings. we are going to sense changes in pain and temperature very soon. even though they are the slowest fibers.
-there is a very different range in which the stimulus can activate these receptors.
-thermoreceptors: important cause organisms need a certain temperature to survive in any environment. (homeastasis: constant conditions for life.)
-internal temperature of body -> 37°C. environment -> 24-25°C. we need to sense both internal and external temperature. (respectively -> internal and peripheral thermoreceptors in the skin).
-the peripheral thermoreceptors' range is much wider as the temperature may change while it shouldn't change with the internal ones. -there is a comfort zone (neutral-> neither hot or cold: 25-30°C.) comfort zone of an internal is 37, there is no range.
-we will be speaking of peripheral: primary order neurons, c or a delta with free nerve endings. same thing applies to nociceptors.
-in between the various mechanoreceptors and proprioceptors we find the thermoreceptors. some of them reach the epidermis while others are a little deeper in the dermis. the receptive field changes. (area in the skin which receives innervation from the same neuron).
<u>c-fibers are more superficial while a delta usually in the dermis</u>.
-active ion channels are closed at rest and only open in response to a stimulus. instead the passive channels are open all the time. all the sensory neurons have ion channels (which respond in a different way).
voltage gated: for the action potentials
ligand gated: e.g. nicotinic receptor for ach
strech/mechanically gated: for the mechanoreceptors (in the dermis) and proprioceptors (in the skeletal muscle) -> when the tissue stretches the channel opens.

ion channels are transmembrane proteins with several domains, cross many times. in between the domain 5 and 6 we have an ion channel. (not highly specific, good for both calcium and sodium which both have positive charges and both go inside the membrane depolarizing it).
temperature gated ion channels: opens in response to a change in temperature. belong to the family of the TRP channels-> transient receptor potential.

-transitory signals, we only receive the signal when the channel opens). they open in response to 2 different channels. (on one side they are temperature gated ion channels but they are also ligand gated ion channels). they thus open both in response to temperature and to a ligand binding to them.
-structures of proteins changes in response to changes in temperature. (e.g. cooking meat) same thing applies to this proteins in the membrane. conformational change: amino acids move and the channel opens. each one of the channels opens in response to a particular change in temperature. -we have cold receptors and hot/warm receptors.
-25 to 35°C we feel normal, anything less is cold anything more hot. we feel it cause at each temperature there is one particular receptor that opens and another one which closes. that sends a different signal to the cns so they don't feel the same.
-trp channels is a big one, there are 28 different channels, which have further been divided in sub families. all begin with trp but the rest is different.
-many times both a thermoreceptor and a ligand gated channel. (chilli -> spicy, but also feels hot, cause you activate the same receptor) (mint -> it's a flavor, but usually represented as cold, cause it binds to a channel which is a thermoreceptor for cold as well.)

-trpv2 and trpa1 are different families. each sensory neuron (type of receptor) has 1 set of thermoreceptors. cold receptors express -> trpa1. warm receptors -> trpv2. we also have receptors for normal temperatures which have both cold and warm receptors at the same time.
-when you reach a limit of temperature that is dangerous for life we have a mechanism that warns us -> pain. thermoreceptors that detect temperature higher than **45**°C are also nociceptors. or anything below **15**°C also.
-cold receptors can detect a really big range of temperatures, while for warm the range is narrower (30-50°C).
-when something feels normal temperature, comfortable we have both cold and warm receptors sending signals. the moment I feel something is cold I only get the signal from the cold receptors. and so is for the warm receptor. this combination of the two makes it possible to discriminate between something which is hot, cold, or middle.
-the number of action potentials is not the same in all temperatures. for each receptor it's different. reason for which cns knows the difference between 25°C and 10°C. (number of action potentials it receives is different). the neuron could be the same (trp channel) but the number of times it sends the action potentials is different.
-each neuron has a particular range in which it works, for the warm receptors as the temperature increases so does the number of action potentials. when there is the peak of action potentials the nociceptor is activated.
-for cold receptors when the temperature decreases so do the number of action potentials.
-if two temperatures have the same number of action potentials (e.g. 15 and 35) the cns can differ them because in the 15 you get just the signal from the cold while in the 35 from both hot and cold (cause in normal temperature). thus the signal in your brain is not the same. (there is integration of the signal coming from different receptors or only one).
a lot of action potentials -> 25°C
little action potentials -> 5°C
you get three signals: 1) what channel has been opened (cold or warm) 2) number of action potential/second, each frequency corresponds to a range in temperature 3) how many receptors are activated at the same time (only cold, only hot, both).
-both internal and peripheral thermoreceptors send signals to the hypothalamus which is the thermoregulatory center.
-integration: you get many different signals at the same time and you make sense of them.
-in the case of warm thermoreceptors the sensation of pain begins at temperatures higher than 45°C. for cold less than 15°C. (but neural firing stops -> no more action potentials -> cold nociceptor begin sending signals).
-4 groups: cold, warm, receptors for heat and pain (thermoreceptor and nociceptor), receptors for cold and pain.(thermoreceptor and nociceptor). and they are regions where they overlap.
-sending information all the time -> slowly adapting receptors.
-each thermoreceptor has different trp channels in the membrane of the dendrites. if specific for cold -> has trp channels for cold. -the receptor field (area in the skin where we receive the dendrites of the neuron) for cold is bigger than the one for hot in the skin. we don't have the same number of receptor fields everywhere (same for mechanoreceptors which are in greater concentrations in the lips and fingers). we have the most in the skin of the face, then fingers, and

then rest of body. -more receptors for temperature in the skin of face rather than fingers because it's the only part we don't cover usually. -trigeminal nerve is responsible for the face.
-even if spa water is 37 degrees you still feel it as warm, but once you've been there for 5 mins it feels normal -> adaptation -> sensory neuron sends less action potentials in response to the same stimulus. -thus when the thermoreceptors work with innocuous temperature it is possible to experience adaptation.
-at first a change in temperature produces a big increase of action potentials but as the stimulus continues (remember it's a slowly adapting receptor) there is a moment in which the number of action potentials is constant. -we have a **phasic** (when temperature changes) and a **tonic** (sustained and constant level of temperature) response. -if the temperature is colder than usual the cold receptor is activated and the warm one is deactivated at that moment (it feels colder than what it actually is) suddenly. it's an abrupt feeling that slowly warns off as the warm receptor is re-activated. (tonic response where both send the same signal). thus if you change the temperature suddenly that feeling is more abrupt than if you change it gradually. this is done to increase the contrast when there is a change in temperature so you feel it really fast. (cause they are slow fibers so we have mechanism for the signal to create contrast). we adapt to a stimulus it if is sustained and if it changes another phasic response occurs instead.
phasic response: when the stimulus is changing, one receptor is activated and the other is silenced, the contrast is high. they behave in the opposite way. it just happens in the regions where you have both of them.
tonic response: stimulus is not changing, receptor is adapted, combination of the two that feels normal.
-adaptation only possible if within the normal range of temperature (not painful). if not you start activating the nociceptors.
-each fiber (whether cold or warm) has it's own peak of activation, depending on the temperature.
-receptive field is bigger for cold (neuron with more dendrites), not the number of receptors.

-trp channels are not specific just for one ion, they are non selective, but mostly for calcium and sodium. (which enter and depolarize the membrane)
-the cells of the immune system are making molecules to fight the infection (e.g. interleukins, cytokines…) which also activate this channels -> reason for which we experience fever when we have inflammation.

-**trpA1** -> cold **nociceptor**, also activated in inflammation.
-**trpm8** -> responds to **menthol**. (reason for which we relate cold to mint) activated with temperatures below 26°C (**not pain, normal cold receptor**).
-trpV4 -> normal temperature
-nociceptors when temperature higher than 45°C.

-cold thermoreceptors: 3 important ion channels for cold trandsuction: **trpM8, trpA1, Nav1.8** (doesn't belong to trp family, it's a sodium voltage channel).
noxious cold (painful) begins at temperatures lower than 15.
nav1.8 -> particularly good for nociception in response to cold.
-frequency of action potentials per second is different between cold and warm receptors.
-the number of receptors that are sending the signal also changes (a lot of receptors sending the signal if the temperature drops more than 10°C.) -thus, the more the temperature drops, the more receptors send the signal but with less action potentials.

-pricking pain vs burning pain: **burning** pain -> sent through **c fibers** ; **pricking** pain -> **a delta** fibers.
for hot receptors:
-there are type 1 and type 2 a delta fibers. if you just say "type 1" you could get confused with a-alpha fibers. type 4 is c fibers, type 2 is a alpha and a beta. type 3 is a delta.
-nociceptors and thermoreceptors can only be c or a delta, if we are talking about a delta it could be both type 1 a delta or type 2 a delta.
-the response to pain between type 1 and type 2 a delta is different. **type 1 a delta** fibers will be responsive to high heat (temperature **above 53°C** -> burning pain). **type 2 a delta** fibers respond to lower heat changes (higher than **45°C-up to 50**)

-the 3 receptors for warm are all TRPV.

trpV1 -> **type 2** a delta -> pricking pain (higher than 43-45°C) sense really fast, but then it stops
trpV2 -> burning pain -> **type 1** a delta (higher than 53°C) dangerous and really painful, signal doesn't stop here, keep touching -> burns even more. takes longer to achieve (delayed) but signal is higher.
trpV4 -> not specialized in nociception -> normal indifferent temperatures. not a nociceptor.
-the signal between type 1 a delta or type 2 a delta is not the same as one is for burning pain and another is for pricking.

-cold receptors don't have type 1 and type 2 a delta. you can easily discriminate if burning or pricking cause one is a delta (pricking) and the other is c fiber (burning).
-warm receptors instead we feel pain with the a delta fibers. and here we have type 1 (burning) and type 2. (pricking) we also have c fibers in warm receptors and they can detect a wide range of temperatures, reason for which we can experience sensitization, fatigue, adaptation etc.

-the interneuron makes a decision according to the stimulus he receives from the sensory neuron.
-in sensory neuron which are unipolar or bipolar the soma is not in one of the extremes but somewhere in the middle of the axon.
-unipolar: one process only. **bipolar**: **soma** in the **middle** with **axon on one side** and **dendrite on** the **other**. -most of the sensory neurons in the body are unipolar, but we have a few bipolar. (e.g. in the retina).
-the free nerve ending is the dendrite, and immediately below it is the axon. you don't see the soma (e.g. if you're touching something with your finger) because it is in the dorsal root ganglion in the spinal cord. (you don't see it in the section of the skin). or in case of the nociceptors of the face, the soma would be in the trigeminal ganglion.

the somas of the proprioceptors go into the mesencephalic nucleus not trigeminal ganglion.
the pons is where the axon enters, but the somas are in the trigeminal ganglion which is in the gasser cave.

motor neurons have a very long axon, their soma is not in the trigeminal ganglion but in the motor nucleus (there is just one)
1st order neurons are really long.
the second order neuron is an interneuron cause it processes the information. (it receives the signal from many 1st order neurons). they are small or long but have a lot of synapses.

B fibers are parasympathetic.
most mechanoreceptors are a-beta, most proprioceptors are a-alpha, thermoreceptors are a delta and c.
-Nociceptors are also c fibers or a delta with free nerve endings.
we feel pain to discriminate that the stimulus is not good and we want to run away from it. (e.g. injury). -many physiological responses cause it or occur in response to it (e.g. inflammatory pain).
-if the pain persists in time and isn't related to any dangerous situation -> pathological pain (we shouldn't be feeling it).
-when we get higher than 45 degrees or lower than 15 these are extremes temperatures for the skin, so the thermoreceptor becomes a nociceptor. (specific thermonociceptor) the more you increase the temperature the more signals you get. there are also non nociceptive thermoreceptors. (detect temperature of different ranges only, the more they change the more action potentials but still not specialized in sensing pain, could still belong to the trp family).
-thus, one receptor/transmembrane protein is not necessarily linked to only one stimulus.
-a sensory neuron has more than one trp channel in the membrane.

-nociceptors have very high threshold HT (can detect a wide variety of stimuli, very sensitive) pain in response to temperature, pressure, injury, chemical compounds…
they are considered slow in sending the signal but they're not bad in sensing pain.
-the pain you feel at the beginning is a very fast pain, but the one that comes after is from another fiber. first sharp pain -> a delta fiber. dull pain which persists in time -> travels through c fibers. (fast vs slow pain), you feel pain twice.

-with pain we may experience sensitization (being exposed to the same stimulus several times getting a higher response to the same stimulus or responding to a low stimulus.)

-hyperalgesia: increased sensation of pain from a stimulus that normally provokes pain but we are receiving a higher sensation. there are primary and secondary hyperalgesia.
we can also experience allodynia -> pain in response to a stimulus that normally doesn't cause any pain.

pain coming from outside -> peripheral receptors
pain coming from inside -> visceral receptors

feeling pain in the skin -> superficial somatic pain
feeling pain in the internal organs -> visceral pain. (e.g. blood vessel)
-there are also nociceptors in the muscles, joints, tendons -> deep somatic pain.

-sensory information enters the spinal cord posteriorly (in the **root of the spinal nerves** there is a **dorsal ganglion** with the **somas** of the sensory neurons). the axon enters the spinal cord and synapses with the second order neuron.
-many times we have one peripheral receptor from the skin collocalizes/ is collateral to a visceral receptor coming from another area inside the body. they enter the spinal cord together and synapse with the second order neuron in a very nearby area. -> we feel referred pain.
(e.g. heart attack -> most common question is where do you feel pain? answer would be left arm and not heart. because the sensory neurons of the skin in the area of the left arm enter the spinal cord in the same nerve where the visceral neurons from the heart do -> we confuse these two feelings and feel like the pain is in that other area of the skin cause it goes in the same area of the somatosensory cortex, cause they reach the same second order neuron) [somatic and visceral afferent neurons might reach the same second order neuron -> reach the same area in the somatosensory cortex].
-doctors may know the map of referred pain. (e.g. ureters -> feel pain in the scapula)

-when people lose a limb they say they still feel it. because in the brain you still receive signals from nearby receptors and you're confusing those signals feeling as if the limb was there, whereas in reality you're just feeling the mechanoreceptors of the nearby area. this is because of the way we synapse with the second order neurons.

-the perception of pain is subjective. the threshold is different in each one of us, even in women vs men. (women are stronger for biological reasons -> children)

-there are ways to block the pain sensation which we need in order to survive. (patient with severe burns needs to replace the bandage everyday so that the injury is clean and heals properly, when you do that it's extremely painful because all of the nociceptors are activated).
sometimes the painkillers are not working anymore or if they interfere with the treatment we need to look for something else -> watching or playing a video game -> distraction which interferes with the perception of pain. the nociceptors are sending the signal but we are blocking it by interfering with it through a distraction.
(e.g. distracting children talking about something else while performing the anesthesia so they are distracted and they don't feel the sensation as much). meditation, acupunture, or motivation might also help. (labor because of motivation -> endorphine release to reduce pain).
-it also works the other way around -> if you expect something to be painful you can make it feel worse.

-trigeminal nerve is where we receive pain sensations from all the skin of the face. (most of it-> specially maxillary and mandibular regions of interest to dentists)
-nociceptors are polymodal (different stimuli able to perceive).
-in any nerve with nociceptor the first order neuron is the nociceptor. (soma has to be in a ganglion: spinal cord -> dorsal root. face -> trigeminal ganglion).
-sensory neurons may have axons that brach -> axons collaterals.

-normally inflammatory mediators released in a normal inflammatory reaction: prostaglandins, bradykanins, interleukins. when they bind to the nociceptor they're gonna activate it -> feel pain. ligands of immune reaction -> inflammatory pain. mediators that interfere with the opening and closing of the channels of the nociceptors. (more or less pain).

-in all the sensory neurons the dendrites have ion channels. when it opens the ions flow and we depolarize the membrane. for the mechanoreceptors and proprioceptors we have stretch gated ion channels. for the thermoreceptors -> temperature gated ion channels.
nociceptors -> high threshold -> milions of ions channels -> possibility to feel pain really high. (huge family of transmembrane protein ion channels).
sometime one trp channel is very specific to one type of stimulus (e.g. specific **mechanonociceptor**/mechanical nociceptor -> nociceptor which only responds to stretching. still **a delta** fibers generally.) it doesn't work in response to other stimuli (e.g. temperature increase or acid burning).
-there are also **polymodal receptors** though. these are usually **c fibers**.

-in the dendrites there are the ion channels while in the axon there are voltage gated channels of sodium and potassium. the threshold of activation is due to the channels they have in the dendrites.

-one nociceptors expresses different types of ion channels.
-nav: voltage gated sodium channels. typically expressed in nociceptors. one of them is a thermoreceptor.
-acid sensing ion channels ASIC -> for acid detection.
-inflammatory mediators -> ligand gated ion channels. (also for atp, neutrophils..)
-all these different ion channels have in common the fact of being active. (at rest it is closed, don't have spontaneous activity and only open in response to the stimulus.) polymodal receptors have several channels at the same time.

-nav1.7 mutations -/- (genetic knockout -> no expression of the gene by neither of the two alleles from mom and dad) is important for nociception. if no expression you don't feel pain.

-there are mechanisms that make an ion channel stay open for a longer time. -> more pain. (sensitivity).
-ion channels look like a tunnel. (e.g.trpa1 -> for temperature)
-calcium voltage 2.2 -> family of calcium ion channels which are expressed in nociceptors.
-g protein coupled receptor (**GPCR**) is **not an ion channel** but another type of transmembrane protein. when a ligand (e.g. inflammatory mediator) binds to it we have a signaling cascade inside that leads to the release of a second messenger (e.g. calcium, cAMP, ip3phosphate….) which causes one of the ions channels to stay open for a longer time than usual. -> sensitization -> more pain than usual. (inflamed gums feel more painful than normal gums). other receptor similar to gpcr is the tyrosine kinase one.

sensitization occurs because besides the ion channels that are specific for nociception we have other channels that can interfere with opening and closing of the channels for nociception.

the membranes of nociceptors express different types of channels in response to different stimuli.
-gpcr receptors and similar ones change many things: the amount of time the ion channels stay open (sensitivity), the amount of channels expressed in the membrane (amount of proteins synthesized when the gene is translated). thus more channels or open for a longer time.

fast pain: sharp, intense, but short. a delta fiber. aka as PRICKING pain. (e.g. electric pain)
slow pain: stays longer in time. c fiber. aka as ACHING, throbbing, slow burning, chronic, dull, nauseous.
not needed to know -> 80% of the nociceptors in the pulp are slow c fibers. 20% a delta.
-with **a delta** being faster, we are able to notice very well where the pain is coming from. **smaller receptor field and greater two point discrimination**. usually for c fiber the receptive field is bigger so you can't tell exactly where you're feeling the pain. both of them are nociceptors and have a high threshold but if you compare them the **threshold is higher for C fibers**.

-mechanoreceptors have big somas and a beta fibers with a lot of myelin. or even a alpha -> large soma.
-nociceptors: smaller soma than mechanoreceptors, they have c fibers and a delta, thus less myelin -> soma usually smaller.
-in ganglions you have the somas of all sensory neurons, they are mixed but a little organized.

-polymodal nociceptors have a wide variety of channels, they range between c fibers and a delta.

-we have very specific nociceptors and also broad range (polymodal) ones. the sensory neurons have axon collaterals (branch of axon) so the dendrites could be reaching another area.

-only the first order neuron is the sensory neuron. **nociceptors** are **unipolar or pseudounipolar**.
-usually there is a combination of a delta and c fibers, reason for which we feel pain twice.
-for dental pain we also have both c fibers and a delta. (fast and slow pain)
-the first order neuron is capable of sensing pain because it expresses several receptors on the membrane of the dendrites. (e.g. trp ion channels, sodium gated, asic, inflammatory mediators…)
-if pain is coming from body the signal enters the spinal cord (where we synapse with the second order neuron)
-if pain signal is coming from the face most of the times it will go through the trigeminal nerve, the sensory neuron enters in the pons and synapses with the corresponding nucleus with the second order neuron. (**SPINAL NUCLEUS** for pain [and temperature])
-in the **trigeminal ganglion** we find the somas of sensory neurons of the somatosensory system with the **exception** of the **proprioceptors**. (which instead are in the mesencephalic nucleus).

-we can nociceptors in the three divisions cause they three of them have GSA neurons. the somas are in the trigeminal ganglion with the exception of the proprioceptors. the axons enter the pons and now go down because they synapse with the spinal nucleus. (for nociceptors and thermoreceptors)
-we don't have any oral structures innervated by the opthalmic nerve. the superior ones through the maxillary and inferior ones through the mandibular (including the tongue through the lingual nerve, anterior two thirds).
-taste sensation travels through facial nerve.

possibilities for nociception in the head apart the trigeminal:
-**facial** nerve carries nociceptive info from the skin of the mastoid region and the auditory meatus.
-**glossopharyngeal** nerve: pain sensations from **posterior** side of the tongue (including tonsils), tympanic cavity (antrum), oronasal portions of the pharynx. *(glossopharyngeal nerve passes through jugular foramen with X,XI as well.)*
vagus nerve: pharynx and larynx, most posterior part of ear, and external auditory meatus.

descending control: comes from higher brain structures and reaches more inferior areas.

1st order neuron: unipolar or pseudounipolar. only one to be unipolar
2nd order neuron: multipolar interneurons and so is the third order one (one soma, many dendrites, and one very long axon). the soma is in the gray matter, the axon with myelin goes into the white matter. synapses with the contralateral thalamus (crosses).
-1,2,3 belong to the pain pathway.

-the thalamus is in the diencephalon which is made of 100 or more nuclei. we can make connections going into many different locations in the cns at the same time. we don't just synapse with one third order, we can synapse with many more.
-one of the first places where we send info is info about **where** do we feel the pain. (**primary somatosensory cortex** in the postcentral gyrus).
-with peripheral nociceptors you localize pain better than if it was visceral pain. (internal nociceptors).
-when the third order neuron goes from the thalamus to other areas one of them is always the primary somatosensory cortex because it tells me where the signal is coming from. (this is true for all the types of somatosensory receptors) -apart the location it can also determine the intensity (how many action potentials). *"where and how much"*
-in order to determine the type of pain (injury, mechanical damage, temperature… which don't feel the same) we need to connect with another area.
-we also have a very big emotional response to pain. so the limbic system will also receive signals from the nociceptors.
-thus when the signal reaches the thalamus, we send it both up and down. (through descending interneurons). these **descending** interneurons do not belong to the pain pathway (which is just

primary, secondary and third order neuron). these interneurons come from upper regions and reach the area where we synapse with the second order neuron (nuclei). they modulate the pain pathway.
pain modulation: increased -> sensitization (excitatory + upregulation) or inhibition (downregulation -). this happens in the synapse between the first and second order neuron, which is in the spinal nucleus for the trigeminal nerve or in the spinal cord for the spinal nerves. there is usually when for excitation and one for inhibition.

-the synapse with the second order neuron is always down with respect to the place where the neurons for modulation are. (hence the name descending neurons).
-the spinal nucleus (for temperature and pain) can be subdivided into three regions: nucleus **oralis** is the most *superior*, *medial* is nucleus **interpolaris**, most *inferior* is nucleus **caudalis**. most of the nociceptors' signal reach the nucleus caudalis. (thus the majority of the nociceptors synapse with the second order neuron in the nucleus caudalis, which corresponds to the spinal nucleus of the trigeminal nerve.) *nucleus or pars is the same anatomical term.*
-for the mouth the nociceptors reach the nucleus oralis and interpolaris.
-the spinal nucleus begins in the pons then goes into the medulla oblungata and then into the first cervical regions of the spinal cord. the pars caudalis is in the spinal cord.

-the synapse it the pars caudalis takes place in the gray matter-> nucleus. in a transverse section the cells will be organized in **laminae** (1-6). **1 is the outer. 6 is the inner**. the somas of the cell of this region do not only pertain to the second order neuron, we also have small interneurons (multipolar, doesn't have myelin). the interneurons are the ones responsible for inhibiting or activating the second order neuron. (most modulation takes place here,between the first and the second order neuron). in most cases, the one that receives the inhibition or the activation is the second order neuron.
islet cells and stalked cells are interneurons. they are going to synapse with the second order neuron.
islet cells are mostly inhibitory -> they release **inhibitory** neurotransmitters. (e.g. GABA or enkephalins [endogenous])
-**stalked** cells: between lamina 1 and 2, neurons that release **excitatory** neurotransmitters mostly.
-when the nociceptors enter the spinal nucleus they synapse in the laminae **1,2,5,6** with the second order neuron. (by axon collaterals)
-in the spinal nucleus we receive nociception and thermoception mostly, but not only. (never 100% in physiology) [e.g. most of the mechanoreceptors go to the principal nucleus but we have some that go the spinal nucleus, but they don't synapse in exactly the same region].
-**mechanoreceptor** synapse in **laminae 3,6** while **nociceptors** have more areas -> **1,2,5,6**.

-when we synapse with the second order neuron we are going to have many possibilities.
some second order neurons are very good in receiving the sensation of pain -> **nociceptive specific** neurons.
-but some second order neurons receive signals from mechanoreceptors for example. (not specific for pain) -> **dynamic** neurons.
-we have a mixtures of these two. -this is why sometimes the sensation of pain is sharp and very well localized while other times it's not. (also reason for which we feel referred pain).
-if the nociceptor is visceral and synapse with the same second order neuron what you actually experience is that the pain is coming from a peripheral receptor in the skin. [this is why some patients with teeth pain might experience headache]

-the axon terminals of the second order neurons go into the thalamus. it is a relay station of sensory info before it reaches the cortex. (place where the 2nd order neuron synapses with the 3rd order neuron.)
-the thalamus is a **paired** organ (one in each hemisphere) in the **diencephalon**. it is composed of **gray matter** -> contains **nuclei**. (accumulation of somas of neurons in the cns). [approximately 100 different nuclei]. -**4** of these receive the sensation of pain -> **posterior thalamic, ventral posteromedial thalamic, intralaminar, centromedial**.

2nd order neuron goes from spinal nucleus to thalamus, where we can synapse with 4 nuclei
3rd order neuron goes from the thalamus to the cortex

from the spinal trigeminal nucleus the info reaches the cortex

ventroposteromedial thalamic nucleus **reaches** the **primary somatosensory cortex** in the post central gyrus. (accounts for the information of where and how much pain)
the other places where the third order neuron sends info are primarily the **insula** and the **cingulate cortex**, which belong to the limbic system. (emotional brain, really close to the thalamus, and really internal structure of the brain)

gyrus: folds/falls in the brain. gyri plural
sulcus: grooves in the brain
-outside of brain is gray matter, inside is white. there are areas of the cortex where we have interneurons, some of them belong to the limbic system (the most internal ones).
-**hypothalamus** belongs to the limbic system and the endocrine system.
-**amygdala** is also belonging to the limbic system.
-all the structures surrounding the thalamus belong to the limbic system.
-hemispheres are divided in lobes, we have 4 (frontal, parietal, temporal, occipital)
between the parietal and the temporal lobes we have a groove (fold)
-when you separate the parietal and the temporal lobes you're seeing cortex, it's not empty space. this cortex is known as insula and belongs to the limbic system because immediately inferior to this we have the thalamus.
-in a midsaggital section you can't see the insula cause it belongs to the cortex, you would need a para saggital.
-corpus callosum: white matter, where the axons of right and left hemispheres cross. it's not cortex cause it's white matter. the first gyrus immediately superior to the corpus callosum is the cingulate gyrus. (emotions -> limbic system) -everything related to emotions is central in our brain. (in the middle/most protected area of the brain).
-when the information goes to the thalamus, if we are sending it to the primary somatosensory cortex we're going all the way up, and in the way up we can send signals to the limbic system. (we have to cross the cingulate gyrus).

-from the **posterior thalamic nucleus** to the **insula**. we receive the info on the type of pain here.
-the emotional pain sensation instead reaches the **cingulate cortex** and comes from the **intralaminar** or from the **centromedial thalamic** nucleus. (emotional behavior in response to pain)
-pain is not always felt as a bad thing (e.g. several massages) we need to remember which type of pain is causing pleasure and which isn't. we want to memorize it so that if we are exposed the second time to the stimulus we are going to be able to react. (first it reaches the cortex -> you experience. then if you want to memorize goes down to hippocampus.)
-**memory** and **learning** don't happen in the cerebral cortex (where we make decisions), they happen in the **hippocampus**. (from the cortex we have other neurons that synapse with other areas). some people may block a memory cause it causes pain to them.

-reticular formation: group of interneurons which are not located in one specific anatomical place. it is a network of sensory neurons sending fibers to many places (activatory signals). they regulate the transition between sleepiness and awareness. (when you sleep the brain is off but not completely, some of the centers are still working). when you wake up all the brain functions are working, we turn them on by activating the reticular formation (goes everywhere and "turns the lights on")
-the reticular formation also sends info from the nociceptors to the hypothalamus and amygdala (also pertaining to emotional brain). it is never painted in textbooks, just as arrows going in many places it is subjective and we don't know the exact location.
-from the limbic system we may also send impulses to nuclei for reflexes. (motor reflexes)

-the neurons in the spinal nucleus also (besides the thalamus) send collateral branches to other places (e.g. reticular formation)

-the information from the thalamus (third order neuron) is now sent to several cerebral areas. when we get information from all of them -> make up our pain sensation (complex and involving emotions).

-if a receptor has myelin it has a big soma. (e.g. mechanoreceptors)
-when something is painful we have the tendency to touch it/rub it.
-in the skin we have both mechanoreceptors and nociceptors from a same area. they synapse with the same second order neuron in a nucleus. their axons have also axon collaterals (branches), which means they can also synapse with other neurons (e.g. small, multipolar, interneurons with a short axon;which aren't either first nor second order neurons). this interneurons are usually inhibitory (-).
-if you feel pain the inhibitory interneuron is not working. if it does it inhibits the second order neuron. (you will feel less pain)
-if you're feeling pain the nociceptor (c fiber) is activating the secondary order neuron and at the same inhibiting the inhibitory interneuron. (which won't inhibit anymore, making you feel more pain)
-when you touch the area where you're feeling pain you're activating the mechanoreceptors as well (a beta fibers, much faster than nociceptors). -they send signal for touch but they have axon collaterals to the inhibitory interneuron. instead of inhibiting it, they activate it, so if you wrap the area where you're feeling pain the mechanoreceptors are activating the inhibition of pain. (through the inhibitory interneuron we're inhibiting the second order neuron, thus feeling less pain than before). you make the pain signal weaker than before.
-some mechanoreceptors in the hair are a-delta.

-the intensity of pain reaches the primary somatosensory area in the post central gyrus (3a,3b,1,2 -> brodman's areas). in order to reach this post central gyrus the thalamus receives the sensations in the ventroposteromedial nucleus. but since we link pain to emotions there are other regions of the cortex which also receive information. from the thalamus we synapse with 3 nuclei that relay the sensation to other areas (insula, cingulate cortex -> both related to the limbic system [regulates emotions].)
the hypothalamus and amygdala also belong to the limbic system.
-we reach the insula through the posterior nucleus
-we reach the cingulate cortex through the intralaminar and centro medial.
-from the limbic system we can still send signals back to the primary somatosensory cortex, making the pain sensation more complete. besides knowing where and how much we can know the type of pain (burning, stabbing), link it to an emotion and thanks to the reticular formation (no anatomical place, it's a network of neurons going from the brain stem to different areas of the brain and making connections) we have axon collaterals coming from the second order neurons that now reach other areas (which also belong to the limbic system such as the hypothalamus and amygdala.
-if we need to memorize a painful sensation we need to use other areas in the brain such as the hippocampus. (for memory and learning). thus from these areas we can also make connections to other brain structures.

-when there is a synapse with the second order neuron, it can be modulated (changed), by either increasing/reinforcing or inhibiting the synapse. (thanks to an inhibitory interneuron in the middle).
-the inhibitory interneuron modifies the synapse between the first and second order neuron. (inhibiting the synapse). you're going to see only what's happening in the area you're paying attention to. (mechanism works for both sight and for pain).
-if the inhibitory interneuron is silenced it's not working, so we feel pain.
-we can have a nociceptor and a nearby mechanoreceptor in the skin, which also sends signals to the inhibitory interneuron, but depending on the receptor they could activate it or inhibit it.
-gate control theory -> lateral inhibition.
-in normal conditions if you're feeling pain and not touching the area -> the nociceptor inhibits the inhibitory interneuron so you feel pain. but when you wrap the area, touch it gently -> you activate the lateral mechanoreceptor which activates the inhibitory interneuron and we feel less pain. (doesn't disappear completely but there's less).

-**modulation** of pain happens through **descending** mechanisms.

-descending because the information of the second order neuron reaches the thalamus, where we synapse with for different nuclei (meaning we can go to other regions rather than the primary somatosensory cortex), and we go down (as in the case of lateral inhibition -> interfering with the synapse b/w the first and second order neuron). [interneurons which go down to the area of the synapse]
-pathway: from stimulus to cortex. -control: everything that acts to the pathway, modifying what is already there. -modulating neurons don't belong to the pathway but they can influence it.
-second order neuron synapses in the **trigeminal spinal nucleus pars caudalis**. (lamina 1 or 2)

-there are two types (sets) of descending neurons. there is an "OFF" interneuron and an "ON".
"ON" neuron reinforces the synapse -> **increases** the sensation of **pain**.
"OFF" activates the inhibitory interneuron -> feel **less pain**. indirectly.
-if you want to feel less pain you need to inhibit the "ON" (we have an interneuron that sends inhibitory signal to the ON). -we want to activate the OFF (regulated through a double inhibition, cause it has an inhibitory interneuron).
-if we want to activate the OFF we have to inhibit the inhibitory interneuron that regulates it.

-periacqueductal grey in the **midbrain** (**PAG**) and rostral ventromedial region (**RVM)** in the **medulla oblungata**.
RVM is where we have the ON and OFF, and they receive signals from the PAG.
-midbrain is superior to the medulla. (in order: midbrain -pons- medulla).
-**GABA** (*gamma*-Aminobutyric acid) is an **inhibitory neurotransmitter**. (<u>inhibits the OFF neuron</u>)
-it is a GABAergic neuron -> neuron that makes GABA.

-opioid receives signals from the PAG. opioid makes opioids (endogenous neurotransmitters)
-example of opioids we make: enkephalins, endorphins..
-opioids are also inhibitory. family of **receptors for opioids -> μ** (there are also other two)
-there are μ receptors both in the ON cell and the GABAergic neuron (in the RVM).
-if I release an endogenous opioid I am blocking the ON neuron and I am activating the OFF neuron -> feel less pain.
-the OFF doesn't have an opioid receptor μ, it receives the synapse from the GABA, so the GABAergic neuron is the one with the μ receptor.
-so if we release an opioid, it synapses with two neurons (the ON, inhibiting it ; and the GABAergic, inhibiting it -> resulting in the activation of the OFF neuron)
-the OFF neuron is regulated by a GABAergic interneuron which is inhibitory. so we have the inhibit the inhibitory interneuron to activate the OFF.
-when you activate the OFF you're activating the inhibition of pain (in the second order neuron). "double inhibition".
-the OFF neuron receives the signal through a GABAergic inhibitory interneuron and the ON neuron directly. thus, there is a <u>direct inhibition of the ON and an indirect activation of the OFF</u>.
-this is really a lateral inhibition because you're inhibiting laterally a neuron to get the opposite action (activating the OFF).
-the GABAergic neuron is regulated through an opioid neuron.
-the opioid is released into the μ receptor of the GABAergic interneuron, so we have reduced GABAergic activity -> reduced inhibition of the OFF cell -> increased inhibition of pain.
-this is a double mechanism with two sets of neurons (ON,OFF) and we use both of them to feel less pain. it's an efficient mechanism because if one of them doesn't work we still have the other one. (double mechanism)
-when this system was first discovered it was used to make drugs. drugs that bind to the μ receptor mimicking the opioids (e.g. morphine, made in the pharmacy -> binds to the same receptors where the endogenous opioids bind to).
-the drugs are more potent than the endogenous opioids -> reason for which we can get side effects.

-gate control theory: lateral inhibition through a mechanoreceptor when they synapse with the same second order neuron.

-our endogenous opioid (neurotransmitters) stimulate the descending inhibition in different regions. (PAG and others) we use our own blockers (GABA, NA [noradrenaline])

-in response to stress some people feel more pain, while other less. (there is a release of adrenaline)
-this pathway was discovered in the first and second world war. (soldiers were injured or parts of the body lacking). nurses couldn't believe they weren't feeling pain and this was justified by the elevated levels of adrenaline which was blocking the pain sensation through an endogenous pathway.
-> not clear evidence for inhibition of pain, subjective. GABA and opioid mechanism is clear and always works instead. -these two are two mechanisms for pain inhibition.

-more pain in response to the same stimulus -> HYPERALGESIA
-extreme of this is allodynia -> something that is not supposed to feel painful actually does.

-there is both primary and secondary hyperalgesia.
-we're talking about pain felt peripherally in the skin (not common for visceral pain).
-**primary** hyperalgesia -> area of the skin [site of injury] where we usually have red color. (related to vasodilation) usually due to inflammation (tissue breakage -> inflammatory response -> vasodilation -> increase in amount of immune cells -> upon touching feels more painful than usual). non painful stimulus felt as painful. mainly related with cutaneous peripheral pain.
-**secondary** hyperalgesia -> touching in a close-by area (healthy) which is not red/inflammed and still feeling pain. feeling pain in a nearby area where the primary stimulus appeared. related with cutaneous peripheral pain but can also be felt viscerally.

Primary Hyperalgesia: aka peripheral sensitization.
-in response to injury the first thing that happens is vasodilation -> we want the cells of the immune system to reach the area and fight asap. -in the inflammatory response you release molecules (some of them intended for the activation of the immune system cells while others are also vasodilators.)
-vasodilators: histamine, prostaglandin e2, bradykanin (but they also bind to receptors in the nociceptors causing pain). -they are **direct stimulators of pain**: bind to the pain receptor and cause pain.
-"hyper" because we experience **sensitization**: increased response to a painful situation. thus the inflammatory mediators make the nociceptors more sensitive to pain. (serotonin too) they are direct ligands of the nociceptors.
-sensitizers: prostaglandins and interleukins, **substance P**. (neuropeptide released by nociceptors themselves). when a nociceptor is stimulated, many times the same receptor releases substance P, which makes the receptor even more sensitive to pain.
-substance P will also act on other molecules (stimulates **mast cells** to release **histamine** [direct stimulator of pain]). increasing the sensation of pain by also working on other cells. -it is released in the dendrites, but can also be released in the axon terminal on the other side.
-increases capillary permeability, contributes to inflammation, promotes vasodilation…
-primary hyperalgesia is really common. -drugs are both anti-inflammatory and analgesics cause they're related. (e.g. ibuprofen) -paracetamol just analgesic.
-cannabinoid receptors also inhibit pain.

-bradykanin and histamine have a double function: stimulation of pain and also sensitization (they are direct ligands for pain but also increase it's perception in primary hyperalgesia).
-substance p is not a direct stimulator but just a sensitizer. another molecule that is also released in primary hyperalgesia is Calcitonin gene-related peptide (CGRP), works as substance P.

trpv1 -> noxious receptor for hot. activates at 45°. in primary hyperalgesia could start feeling pain already at 41°. (activates earlier) this happens because it has more channels in the membrane and they open faster. [the threshold of activation changes, it's almost open already when it gets close to the stimulus so it takes less time to open it. it's more sensitive than before.] (in response to signal transductions in response to substance P, CGRP, histamine, bradykinin… which modify the gene expression and the state of the channel.)

Secondary Hyperalgesia: aka central sensitization
-allodynia is one type (the extreme) -> we feel pain in an area where we should not.
-in response to a normal non painful stimulus we feel pain cause we don't inhibit it, just touching the area activates pain.

-hyperalgesia is increased response to a painful stimulus, while allodynia is a painful response to a non painful stimulus.
-primary hyperalgesia -> depends on first order neuron. inflammation causes cell to make more action potentials.
-**secondary** hyperalgesia -> depends on the **second order neuron**

-one of the physiological mechanism is **convergence**: similar to referred pain. similar from two first order neurons converge on the same second order neuron. in referred pain you had this with a peripheral nociceptor and a visceral nociceptor (two nociceptors), while in convergence you have this with a nociceptor and a mechanoreceptor in the same area of the skin.
-afferent neurons from the healthy area converge in the same second order neurons that receive the pain signals from the injured area. (you feel pain when you're actually just touching.
-both allodynia and hyperalgesia may be due to convergence. (increased response to a non painful stimulus or an increased response to a painful stimulus).

-the other physiological mechanism is the **facilitation** theory: when the second order neuron gets more activated than usual. impulses from the injured area cause a state of stimulation in the central neurons (increase excitability of second order neuron)
-lowering the threshold by modifying the resting membrane potential of the sensory neuron (from -70 to -65 for instance, making it more positive and closer to -55 -> lowering threshold).

-the external medium is made of sodium chloride. if you open the channels chloride (-) would get inside -> more negative -> harder to get to -55mv. -if instead calcium (+) enters the cells -> easier to reach the threshold cause helps depolarize.

-sometimes we can modify the first order neuron: increasing the number of dendrites -> you respond faster to pain -> smaller receptive field. or increasing the number of action potentials fired.
-secondary hyperalgesia has to do with both primary and second order neurons.

-microglia: phagocytes which take out cellular debris. substance P activates them too.
makes the second order neuron produce nitric oxide (vasodilator) which will support with the positive feedback.
-primary hyperalgesia can finally develop into a secondary hyperalgesia (if the cell starts making more receptors, if they open faster, lower the detection threshold…) the cycle depends on how many inflammatory mediators we have and how long they stay.

NMDA family of receptors: overexpressed in secondary hyperalgesia. if we want to block it we block this receptor. ketamine blocks them. the role of the receptor is to **take chloride out**. (by active transport.)(depolarization help, membrane more positive). **activated microglial** cells increase the expression of this receptor.

GABA receptor is a receptor for **chloride** -> more difficult to feel pain when chloride gets in. (by concentration and electrical gradient).

UNIT 10:

-for mastication you need the coordinated control of several muscles. some of them are innervated by the trigeminal nerve but not all -> motor innervation of the tongue comes from the glossopharyngeal, vagus, and hypoglossal nerves.
-we don't just move the muscles of mastication when we chew. -> we need the facial nerve too.
-the movements of mastication have to be very precise (mandible protraction, retraction, moving up and down).
-the **trigeminal motor fibers** are not in the three divisions, they are just in the mandibular division. they are **SVE fibers**. (special or visceral) not GSE (general somatic efferent) because chewing, swallowing etc. are not completely voluntary. (we don't have to think about chewing all the time to do it correctly). involutary control -> SVE fibers. -we have a double control (involuntary and voluntary).

-if **voluntary** movement order is coming from the **cortex**. if it's **involuntary** it's a **reflex**, and the order comes from an **interneuron**, which can be find in the **spinal cord** or in the **brain stem**.
-if found in the spinal cord -> spinal reflex
-if found in the brain stem -> **cranial reflex**. for the muscles of <u>mastication</u> we're talking about cranial reflexes. (interneurons found in the brain stem)
-for motor neurons we just have one motor nuclei in the trigeminal nerve. it is found in the **pons**. (it is next to the spinal sensory nucleus)
-many times the order to contract a muscle is going to come from a motor neuron (multipolar, with the soma in the trigeminal motor nucleus and the axon which goes through the mandibular division and reaches the different muscles) which receives information from different parts in the brain. (cortex for voluntary and from the same motor nucleus for involuntary control).

-we're going to have different cycles, and everytime we chew we repeat one cycle.
-when the food enters the mouth we feel it thanks to the GSA fibers of the trigeminal.
-in response to this feeling a reflex occurs -> opening the mouth to make room for the food that just entered. **first r<u>eflex</u>** -> **opening** of the **jaw**. (muscles are stretched, proprioceptors will make you feel it). when you stretch a muscle a response occurs, (e.g. when you stretch a ligament of the leg the quadriceps contracts) which in this case is the **second r<u>eflex</u>** -> **closing** the **jaw**.
-after you close the jaw the food is in between the dental pieces, you make it smaller and a new cycle will then begin. (repeats itself)
-this cycle for chewing is just a reflex or sometimes it could be voluntary.
-the consistency of the bolus has to be good enough before we swallow. we need to regulate the process with respect to what we're eating. (e.g. soup vs steak) you feel it with the mechanoreceptors in the oral cavity. you adjust the contractions of the muscle with respect to what you're feeling. (is the bolus ready or not).
-thus there is also a central control (voluntarily changing the reflex).

-dental patients might have problems with the occlusal plane, which will lead to a poor chewing process.
-before we start eating there is a preparatory phase which is an anticipation mechanism. (salivation) [digestive system getting ready for chewing].
-food contact phase: food enters the mouth (GSA fibers activated, sending activation to 2nd order neuron, which goes to the 3rd and from there to the primary somatosensory cortex) and you know it. in this moment the reflexes begin and the cycle repeats -> crushing phase. (several chewing cycles). -the cycles are not constant (e.g. speed changes -> at the beginning is faster, when the food gets more liquid, speed decreases). -thus we adjust the speed to the consistency of the bolus.
-there is a moment when you send the bolus to the last portion of the oral cavity -> molars to finish with grinding. (reason for which we need the occlusal plane to be good)
-swallowing is also a reflex, which could be voluntarily controlled.
-after we swallow the process begins again.
-mechanoreceptors go to the principal or <u>spinal</u> trigeminal nucleus. just next to the principal is the trigeminal motor nucleus in the pons. we have connections between them through interneurons. (go from the sensory to the motor nucleus).
-soma is in the trigeminal ganglion and the axon is entering in the brain stem where they synapse with the second order neuron in the nucleus. but they can also send the signal through interneurons to the trigeminal motor nucleus.
-principal, spinal and trigeminal motor nucleus are thus connected through interneurons.
-trigeminal motor nuclei have multipolar neurons, with the soma in the nucleus and the axon going through the mandibular division and to the muscle from there.
-in the principal and spinal nucleus we have the axon terminal of the first order neuron and the soma of the second order neuron that goes to the thalamus. and we also have the interneurons which connect us to the trigeminal motor nucleus.
-in the trigeminal nuclei you find the second order neuron's body, and it's axon reaches the thalamus.

-when we need a reflex the order doesn't come from the cortex, it stays in the brain stem. (because we have interneurons that are making connections between the first order neurons and the motor nuclei).

-in response to food we have an **inhibitory** reflex (relax the muscles of mastication to open the jaw to make room for the bolus). this reflex is happening in the **brain stem**.
-once the jaw is lowered the muscles of mastication are stretched. this will be felt by the proprioceptors which will lead to a contraction. (cause it's axons go to the motor nucleus of the trigeminal nerve). [stretch reflex by activating the mastication muscles which close the jaw: rebound contraction]
-once this is performed you completed a single cycle of chewing. it can be repeated many times and the speed can be modified and adjusted depending on what we are eating.
-at the same time this reflex is occurring the cortex is aware that we have the food in the mouth , because the neurons also undergo the normal somatosensory pathway. so since we know that we are eating something, if we choose to, we can modify the reflex.

-the cycle can be repeated many times without us thinking about it (e.g. chewing gum), it is regulated and repeated because we have a **supratrigeminal nucleus** that **regulates** in an autonomic way the **contractions** happening in the **trigeminal motor nucleus**.

-there are many regions controlling mastication in the brain. the information goes to the nuclei (3) and we can have a reflex, or we send the signal to the second order neuron which then follows the normal pathway ending in the **primary somatosensory** area in the post central gyrus. (this tells us **where** and **how much**). from the primary somatosensory area we go to the insula and cingulate cortex. it also may reach the secondary somatosensory cortex, where we will process the information even further.
in a motor pathway from the cortex to the muscle we just need two neurons. (upper UMN and lower LMN motor neurons). we don't go to the thalamus. the soma of the upper motor neuron is in the motor cortex (which is located in the **primary motor cortex**, which is in the **pre central gyrus**).
[in response to things we <u>feel</u> we have movement so the two areas in the cortex are close to each other] -the somas of the lower motor neuron are in the trigeminal motor nuclei in the case of the trigeminal nerve.
-we also have a pre motor cortex to help in the coordination of movement, and other areas…
-in order to coordinate the movements we need to know our position in space so we need the proprioceptors too. -the organ for balance and equilibrium is the cerebellum. -the **somas** of the **proprioceptors** are in the **mesencephalic nucleus** while the **axons** go to two different places -> to the **cerebellum** and to the **trigeminal motor nucleus**. (we need to know our position in order to coordinate movement).

-basal nuclei: composed of gray matter, which is not just found in the cortex. they are internal regions inside the brain with nuclei, and they are very important for the coordination of movements.

-somatotopic representation: map of the regions of the body that are represented in one part of the cortex. "homunculus" -> somatotopic representation of the skin.

-**GSA** fibers in the **oral cavity** go to the **<u>lateral</u>** part of the **post central gyrus** in the primary somatosensory area.
-the area that controls **chewing** and **mastication** in the **primary motor cortex** (cortical primary masticatory area) of the <u>pre central gyrus</u> is also **<u>inferolateral</u>**. (both for primary somatosensory and primary motor).
-this (cortical masticatory area) is where you have the upper motor neuron's soma (in the cortex), and the axon (with myelin, white matter) goes down to the trigeminal motor cortex.

-several **axons** together **outside** the **cns** -> **nerve**
-several **axons** together **inside** the **cns** -> **tract**

-thus the axons of these neurons make the <u>corticobulbar tract</u> through the cortical masticatory area. (begins in the cortex -> "cortico" ; reaches the **medulla oblungata** -> "**bulbo rachideo**")
-as a matter of fact for chewing we don't just use the motor neurons from the trigeminal nerve, we also have the neurons of CN XII -> moves the tongue ; CN VII -> facial muscles.
-upper motor neuron begins in the cortex and the last nucleus is in the medulla oblungata.

-lower motor neuron is multipolar and goes from the nucleus to the muscle (of tongue, face, mastication)

-the whole tract is the axons of all the neurons that synapse with the lower motor neuron. some of them synapse in the **trigeminal nucleus** for the **muscles** of **mastication** while some of them keep going down, the **last one** is for the **hypoglossal** (**tongue**) which is in the **medulla**. the tract begins in the cortex and finishes in the medulla.

-in the **somatic motor pathway** we have two possibilities: **direct or indirect**.
direct -> begins in the cortex (corticospinal or corticobulbar)
muscles from the neck or inferior -> corticospinal (because neuron goes from cortex to the spinal cord and it synapses with the lower motor neuron.
corticobulbar: if movement of the head (staying in the brain stem). includes cranial nerves: III,IV,V,VI,VII,IX,X,XI,XII.
-if the order is not coming from the cortex it doesn't begin with "cortico" and it is an indrect pathway.
-upper motor neuron: soma in the primary motor cortex (pre central gyrus, masticatory area), axon in the corticobulbar tract. synapses with the lower motor neuron in a motor nucleus. (could be trigeminal, facial or hypoglossal [cause you have the muscles of mastication, of the face, and of the tongue working together]) and in the motor nucleus we synapse with the soma of the lower motor neuron. (and then the 3 lower motor neurons go to the muscles)

-in the **corticospinal** pathway if you move you're **right hand** the order is really coming from your **left** cerebral **hemisphere**. doesn't work like this in the **cortibulbar** pathway. (**head**)
-in the head we receive signals from the upper motor neurons in the two sites. (there is no crossing over, we regulate the muscles on the two sites together). we send signals to the right and to the left muscles, so we coordinate both at the same time if we want to.
-so we can modify voluntarily the orders of the lower motor neuron from the cortex. (chewing is a reflex but we have control over it if we want to) [there are areas in the brain that send orders down to the lower motor neuron that is responsible for contraction]

-if you look at the corticobulbar pathway, and you just look at the corticotrigeminal (just staying in the trigeminal motor nucleus), you can see that you have axons of neurons going to both sides (bilateral and contralateral projections of the neurons).
-the reticular formation makes connections from the brain stem to many different regions of the brain. there are also connections between the motor nuclei and the reticular formation.

-the reflex can be modified in a voluntary way, but it has to be done in a very coordinated way because the chewing movement is smooth and in a sequence (they are not sudden contractions)
-they happen smoothly because there are neurons that control the beginning and the finish of this contraction. we can adjust it to the things we feel (somatosensory), until the bolus is ready for swallowing (different depending on which food). we need a fine control of movement.
-the upper motor neuron needs help, will receive signals from other parts of the brain. this is where the basal ganglia (BG) kick in. (help the upper motor neuron to have a voluntary control on the chewing reflex)

Anatomy of basal ganglia:
also known as basal nuclei, areas of gray matter deep in the brain, not peripheral like the cortex, they are inside and close to the thalamus (in the diencephalon). they lack a regular shape (even do a spiral). there are 3 basal ganglia, involved in the control of movements. (coordinated ones, not only chewing, they coordinate movements of the whole body)
-3 basal ganglia-> **caudate**, **putamen**, **globus pallidus**
-caudate: inferior and lateral to the lateral ventricle. it's the first basal nucleus and most medial of the three.
-globus pallidus is the most internal one with respect to the putamen. (most medial of the lentiform nucleus)
-putamen is the most lateral with respect to globus pallidus.
-since the putamen and globus pallidus are so close to each other we refer to them as one -> **lentiform nucleus**.

-the related ones physiologically (function-wise) are the caudate and the putamen. the name for them is **corpus striatum**.
-the globus pallidus has two regions: one is more internal and the other one is lateral.

-there are two other regions (associated structures) of gray matter that work with the basal nuclei. so related that some books regard them as belonging to the basal nuclei. they are the **subthalamic nucleus** and **substantia nigra**.
-the subthalamic nucleus is inferior to the thalamus.
-in the midbrain (a little lower than the thalamus) there is the substantia nigra. called so because the neurons here have melanin which gives them a black color.
  -it also has two regions, which have different neurons -> **pars compacta** and **pars reticulata**

-the upper motor neuron has the soma in the cortex and it's axons reach the corticobulbar or the corticospinal tract. it doesn't work alone: receives many signals, processes them, and makes decisions according to them. (it's like a police man controlling traffic, looks in all directions to make decisions, he's getting signals from everywhere to make the order) this way we can coordinate movements without voluntarily thinking about it.
-the upper motor neuron makes the orders and can change them upon being influenced by the other signals it receives. one of the places it receives signals from is a circuit made by the basal ganglia. neurons from other regions of the cortex (e.g. temporal or frontal cortex) send information to the basal nuclei. you can also get signals from the cerebellum. and all these signals go to the **thalamus**, where we have a neuron that finally goes back and sends information to the upper motor neuron. [parellel circuit/circle: the info goes down and then comes back up and have to possibility to change what happens in the upper motor neuron]
  -before we go back we must go to the thalamus.

-information that enters and leaves the circuits of the basal ganglia modulates **cortical efferences** (upper motor neuron). they regulate the generation of the movements of mastication so they happen smoothly and not suddenly. they also regulate the muscle tone for specific movements and can also regulate the subconscious chewing reflex (which happens in the supratrigeminal nucleus).

-when the upper motor neuron gets **signals** from any area of the cortex all the signals **enter** the **corpus striatum**. (input: information entering must go through the corpus striatum)
  -from there we send the information to the globus pallidus and we start making connection with the other areas.
-there is a **double exit** for the information: **internal globus pallidus** and the **substancia nigra pars reticulata**. (output to the thalamus) [most basic and shortest circuit]
-when we also get info from the substancia nigra pars compacta and from the subthalamic nucleus which make the circuit longer.
-the **corpus striatum** receives info from the **substancia nigra pars compacta** as well and the **globus pallidus** from the **subthalamic nucleus** as well.
-some neurons that make connections are excitatory while others are inhibitory, and some of them are both. (we need to know the neurotransmitter they release)
-**inhibitory** -> release **GABA** (-)
-**exctitatory** -> release **glutamine** (+)
-**dopamine-releasing** -> depending on the receptors (d1 or d2) it binds to could be both excitatory or inhibitory. the dopamine releasing neurons are found in the **substancia nigra pars compacta**. (no sign +/-) the result is going to be the activation or the inhibition of the post synaptic neuron.

-from the many regions in the cortex to the striatum (input) -> excitatory
from the corpus striatum you can send the signal to the globus pallidus or the substancia nigra pars reticulata. (output, shortest circle you can get, globus pallidus internal.)
-the neuron in the corpus striatum releases GABA (inhibitory). and so does the neuron in the output. -there is the possibility of a double inhibition.
-globus pallidus external is inhibitory.
-subthalamic nucleus is excitatory.

-substancia nigra pars compacta is both.

-the imput is not just received from the motor cortex, also from the substancia nigra pars compacta. there is no input from the spinal cord. it can also come from an association area (association visual/olfactory area), they don't have to be close, could be from other neurons in the cortex. -the information is sent to the basal nuclei. (input to striatum).

-we have two places for the control of movements because we have one movement that we need to coordinate a lot because we are moving it all the time -> the **eye**. (comes from the **substantia nigra pars reticulata**) while for the rest the internal globus pallidus.

tonic interneuron: active at rest, sending action potentials but doesn't need a neurotransmitter to do so. globus pallidus is tonically active. so if the corpus striatum is at rest (not releasing gaba when nothing happens), there is no inhibition of the globus pallidus which sends inhibitory signals (releasing GABA) to the thalamus so that there is no excitation of the upper motor neuron (no contraction of the muscle).
-if instead we want to contract the muscle we activate the corpus striatum and the neuron releases GABA, which inhibits the neuron in the globus pallidus (stops sending action potentials for a period of time, and not releasing GABA), thus not inhibiting the neuron in the thalamus -> we send the order to contract the muscle.

-when you enter the circuit of the basal ganglia sometimes you finish and that's it but other times for more complex movements the cycle repeats (so you reach both the corpus striatum and the cortex). you reach the striatum as well as the motor cortex to inform the striatum about what's going on in case you need to repeat the movement (without having to receive the initial input again -> faster)

-the mastication reflex is modified (speed/strength) by the basal ganglia. [central pattern generator]

-the cerebral cortex is the area of gray matter which is peripheral in the cerebrum. we have interneurons here that receive information, process it, and make decisions. it is organized (just like everything in the cns). we organize it in both sides of the central sulcus (that separates the frontal from the parietal lobe). everything that is dorsal to the central sulcus is mostly sensory and everything that is ventral or anterior is motor. in the central sulcus we also have the primary somatosensory area (post central gyrus) and the primary motor cortex (pre central gyrus). in these areas we get information about **where** we feel the sensation (primary somatosensory cortex) and what part of the body you're moving (primary motor cortex). [reason for which you can draw the map for the regions of the body that receive information]. -there are areas which correspond (e.g. oral cavity is inferolateral in both maps) between the two cortexes but also areas that differ.

association areas: where you associate something with the meaning. (e.g. the sensation of vision reaches the occipital lobe (primary visual area), and next to it there is an association visual area. we see the object in the primary visual area, we know what the object is in the association visual area (e.g. a water bottle).

-association areas together with basal ganglia are going to be important for coordination of movements. (seen earlier for the control of mastication)
-control of mastication -> control over a reflex which is the combination of opening and closing the jaw. pattern which can me modified (speed, strength), or stopped when we decide to swallow. we thus need input signals about what is happening. this input derives from the GSA fibers (mechanoreceptors, proprioceptors, thermoreceptors, nociceptors) of the trigeminal (for the oral cavity). principal and spinal nucleus of the trigeminal receive the info for touch, temperature and pain. it is here that the neurons synapse with the second order neuron, move to the ventroposteromedial nucleus in the thalamus and from there the 3rd order neuron goes to the primary somatosensory area in the cortex.
-proprioceptors in muscles are important because we need to know the position of the muscle to control the strength of the contraction. their somas are in the mesencephalic nucleus and the axon goes to the cerebellum (to maintain balance and equilibrium, signal will reach the pre motor cortex) and motor nucleus. -we have two areas in the cortex involved (one frontal -> motor and

one dorsal -> sensory) and they will join the cortical primary masticatory area which is found in the inferolateral motor cortex.

-the output of the basal ganglia is the substantia nigra pars reticulata and the internal globus pallidus. but before the information leaves we have the possibility to receive information from the subthalamic nucleus as well. when the signal leaves from the circuit of the basal ganglia it has to go through the thalamus first. (mandatory) there is no output directly from the bg to the cortex.

-interneuron with the soma in the thalamus. the axon with myelin in white matter and the axon terminal in the cortex. this final interneuron sends always information that we have regulated in the basal ganglia to the cortex (to the upper motor neuron), which is capable of modifying the signal according to what is happening in the basal ganglia.
-shortest pathway -> motor area-input -output -thalamus. not the only possibility cause we have other areas which also receive signal (e.g. subthalamic nucleus sending signals to the output or the external globus pallidus which modifies this pathway). -and also the substantia nigra which could inhibite or activate the striatum.

-complex loop that may lead to the activation or inhibition of movement depending on the signal that we get.
-the neurons that go from the input to the output are GABAergic (inhibitory)

-the eye movement is highly coordinated, we have 3 cranial nerves involved in it's movement.
-from the input of basal ganglia one of them is specialized in the anticipation of the movement of the **eye**. ->**caudate** nucleus (receives information from the areas that control the movement of the eye)
-the putamen instead is for the rest of the body.
-insula and cingulate cortex (both limbic system) are related to the basal ganglia. so these loops in the bg don't just control movement.

-once we integrate all the information it leaves the circuit of the basal ganglia through the output structures: substancia nigra pars reticulata (for the eye) and the internal globus pallidus (for the rest of the motor movements).
-the two output structures which send signals to the thalamus are also inhibitory (GABAergic).
-the neurons from the cortex to the input are excitatory usually (release glutamate).

-if we don't want to move, we don't send signals to the corpus striatum (A). thus it doesn't release GABA, so there is no inhibition of the neuron in the globus pallidus (B). B is a tonically active inhibitory interneuron. when resting it's sending action potentials (opposite to the concepts studied in neurophysiology before where you release an action potential in response to stimulus).
-thus if there is no inhibition of B by A, B will release GABA all the time. -> will inhibit the neuron in the thalamus. -> no movement from the cortex.

-if we want to move, we receive signals from other areas in the cortex (e.g. motor area), the neurons from the cortex will excite A (which is GABAergic, will release GABA) -> inhibiting B (which is tonically active, but as long as GABA is there it stops firing action potentials) [transient inhibition for as long as A is releasing GABA]. -so B won't release GABA to C -> will be active and send the signal to the cortex -> we move.

both A and B are GABAergic, but B is tonically active. (sending action potentials at rest). so we actually move when we receive a signal from the cortex which leads to the inhibition of B by the activation of A.

-the thalamic neurons (C) are activated by other neurons which are excitatory and reach the thalamus. -C is normally inhibited in the absence of movement because even if these excitatory neurons reach it, there is B which is inhibiting it.

-by this system we may control the initiation and the stop of the movement. (for the shortest pathway)

-motor neurons in the motor cortex (D) -> induce the activation of motor circuits.

-in the substantia nigra pars **reticulata** we control the movement of the **eyes**, this happens in the **superior colliculi** which are **posterior** in the **midbrain**. (it's a gray matter area for the movement control of the eyes)

-more than 100 neurons in the striatum send signals to one cell in the globus pallidus. (able to integrate signal from 100 cells). [convergence of signals]
-when the signal leaves in the output, we are considering many regions at the same time. thanks to this we can prevent unwanted movements and control the initiation and stop of a motor movement very well.

-from the internal globus pallidus the signal goes to the **ventroanterior**, **ventrolateral**, centromedial thalamic nuclei. (signal used mainly to prevent movement we don't want to do). it can also receive signal from the substantia nigra pars reticulata.
-from the substantia nigra pars reticulata the neurons reach **mainly** the superior colliculi. (to prevent the movement of the eyes). some of the signal also goes to the thalamus. (colliculi are in the midbrain)

-the internal globus pallidus may also receive signals from the external globus pallidus.

-two ways to leave the basal ganglia: direct and indirect pathway. (antagonist/opposite)
-if you enter one pathway you're gonna initiate movement while if you follow the other you're going to stop the movement.
-direct pathway facilitates the initiation of movement, whereas the indirect suppresses inappropriate movements. sometimes you get signals from both, but you listen to the stronger.
-the substantia nigra modulates them, cause it has the dopaminergic neurons. (profound influence on the corpus striatum [input]). determines which pathway you will take.

direct pathway: cortex -> striatum (A) -> internal globus pallidus (B) -> thalamus (C) -> frontal cortex [motor] (D)
-shortest. -highly regulated through the substantia nigra pars compacta. if we want to **reinforce** the direct pathway the neurons of the substantia will release **dopamine**, which will bind to the neurons with the **D1 receptors** in the striatum. (D1 is excitatory/activatory)
-A is receiving signals from the cortex and from the dopaminergic neurons. -> will get excited, releasing GABA to B which will be transiently inhibited. (B not releasing GABA) -> thalamic neuron (C) which integrates excitatory interneurons from other areas becomes active and the movement begins. (facilitates initiation of movement)

indirect pathway: when the signal comes from other areas (substantia nigra pars compacta, external globus pallidus, subthalamic nucleus) we activate the **D2** receptors for dopamine, which are inhibitory. (inhibit the direct pathway-> suppression of movement). -neuron A inhibited. (GABAergic -> no release of GABA -> no inhibition of the tonic interneuron B)

-**subthalamic** nucleus neurons are **excitatory** (release glutamate). they excite B which is inhibitory -> no movement.

-degeneration of neurons: lose myelin, die, lose parts of the axon (not able to replace them), cns has the ability to regenerate but there is a limit. (when a neuron degenerates completely it is not possible to replace it). when this happens in a high number of neurons they lose their ability to perform their role. if this happens in the basal nuclei you get diseases related to uncontrolled movement. (e.g. huntington disease -> people move a lot and can't stop ; parkinson disease -> uncontrolled movement of the lips) -if they think about stopping they can't because the order is coming from the basal nuclei. -hemiballismus also a hyperkinetic disease.
-in each of the 3 disease the neurons responsible are in a different location.
-**huntington**: **external segment** of the **globus pallidus**. influencing the **indirect pathway**.

-in the absence of the normal inhibitory input from the striatum, the external globus pallidus are abnormally active and sending information to the motor neuron the entire time. -> uncontrolled movement.

-**parkinson**: neurons affected are from the **substancia nigra pars compacta** (*dopaminergic*). it's difficult to treat because we can both suppress or promote the movement through these neurons depending on the receptors they bind to. -we lose the dopaminergic neurons. (can't regulate the inhibition or activation of the striatum) -influences the **direct pathway**.

-**hemiballismus**: damage in the **subthalamic nucleus** (also influencing **indirect pathway**).

-the basal ganglia apart from influencing areas of the frontal lobe (motor) might involve areas which are not primary motor areas. (e.g pre frontal loop and limbic loop)
-we don't just get signal from the motor cortex and we don't just regulate motor movements. the are some circuits which are non motor basal ganglia. they will reach different areas of the cortex. (e.g. cingulate cortex/insula/dorsolateral pre-frontal cortex)
-thus basal ganglia might be related to the beginning and end of other mental processes. (e.g. memory, learning, motivation) -this might justify that patients with parkinson start experience problems with emotions, memory and behavior.