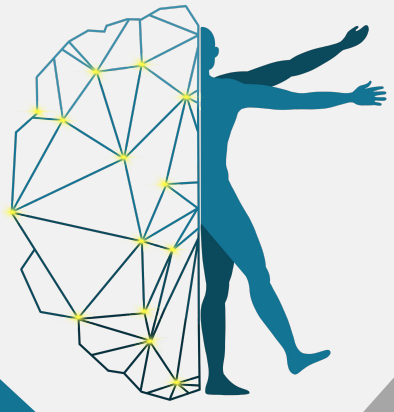
Physiology Team 439

MED439
KING SAUD UNIVERSITY



Mid Term Revision

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Disclaimer

This file is a students effort. it is **NOT** a source to study from. study your slides carefully then check this file please and make sure you cover the important things that we obtained from doctors. Some points we need to clarify:

1- Prof.Meo's revision is **NOT** included in this file.

2- There are tremendous differences between the boys and girls slides. Make sure you cover them both.

3- We highly recommend that you study the teamwork since the best students work on it.

Good Luck

Physiology of Motor Tracts

Motor Areas

R

1 The Primary Motor Area (M1 Motor area 4):

❖ Occupies the precentral gyrus & contains large , highly excitable Betz cells, anterior to central sulcus, Betz cells are also called pyramidal cells

❖ M1 of one side controls skeletal muscles of the opposite side of the body. Left motor area innervate right body side and vice versa

❖ Feet are at the top of the gyrus and face at the bottom , arms and the hand area in the mid portion. Inverted

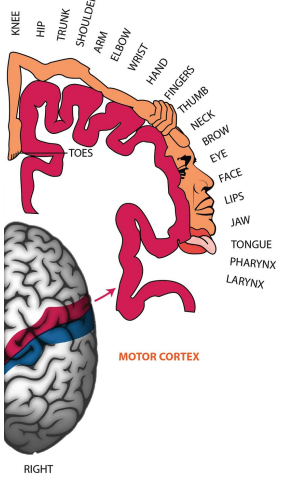
❖ Facial area is represented bilaterally, but rest of the representation is generally unilateral.

❖ Area of representation is proportional with the complexity of function done by the muscle. So, muscles of hands and speech (lips, tongue , and vocal cord) occupies 50% of this area

❖ The neurons of this area arranged in vertical Columns. Each column has six distinct layers of cells, The pyramidal cells that give rise to the to the corticospinal fibers all lie in the fifth layer.

❖ The Betz cells fibers transmit nerve impulses to the spinal cord at a velocity of about 70 m/sec, the most rapid rate of transmission of signals from the brain to the cord.

❖ Betz cells axons send short collaterals back to the cortex to inhibit adjacent regions of the cortex when the Betz cells discharge, thereby "sharpening" the excitatory signal.



- Generally focus on functions of each one and make sure to differentiate between the motor areas (1,2, and 3)
- Focus on Betz cells and know that they have a high conduction velocity **AND** Minimum synaptic delay

2 The Supplementary Motor Area (M2):

primitive type of movements.

❖ located on the lateral side of the brain in front of area 4 and above the pre-motor area & extends on medial side of the cerebral hemisphere.

❖ Concerned with planning ,programming and organizing motor sequences.

❖ Stimulation of this area leads to bilateral (bimanual)grasping movements of both hands simultaneously.Example:playing piano

❖ This area make motor programs for axial muscles. It provides background adjustment for finer motor control of the arms and the hands by the premotor area and primary motor cortex

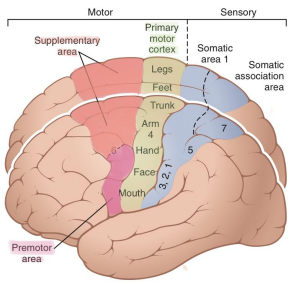


Figure 56-1. Motor and somatosensory functional areas of the cerebral cortex. The numbers *4, 5, 6,* and *7* are Brodmann's cortical areas, as explained in Chapter 48.

Motor Areas

R

3 The Premotor Area (M3):

skills and learned type of movements.

❖ lies in front of the primary motor area & below supplementary motor area.

❖ Stimulation of the premotor area produces complex coordinated movements, such as setting the body in a certain posture to perform a specific task. Steady position . مسؤولة عن الحركات المعقدة زي الكورشيه

❖ It works in association with the supplemental motor area, establishing the motor programs necessary for execution of complex movements.

❖ It contains mirror neurons which are important for understanding the action of other people and for learning new skills by imitation.

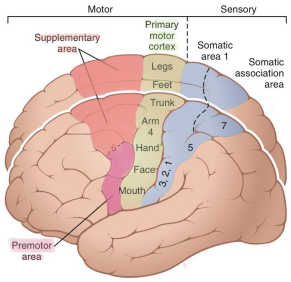


Figure 56-1. Motor and somatosensory functional areas of the cerebral cortex. The numbers *4, 5, 6,* and *7* are Brodmann's cortical areas, as explained in Chapter 48.

A few highly specialized motor centers have been found in the premotor areas of the human cerebral cortex:

Premotor Area	Location	Function
Broca's Area for Speech Damage to this area can cause Broca's aphasia (motor aphasia or aphemia)	Broca's Area	Speech
Frontal Eye Movements Area	Above Broca's area in the frontal lobe	Controls voluntary movements of the eyes toward different objects in the visual field
Head Rotation Area	Above the Eye movement area in the motor cortex	Directing the head toward different visual objects
Hand Skills Area Damage to this area causes motor apraxia (motor disorder in which the individual has difficulty with the motor planning to perform tasks or movements)راح يخسر الحركات الدقيقة	Above the Head rotation area	Hand Skills

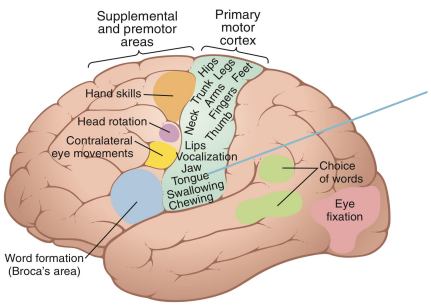


Figure 56-3. Representation of the different muscles of the body in the motor cortex and location of other cortical areas responsible for specific types of motor movements.

If we stimulate this area the patient will produce unmeaning words

Motor tracts

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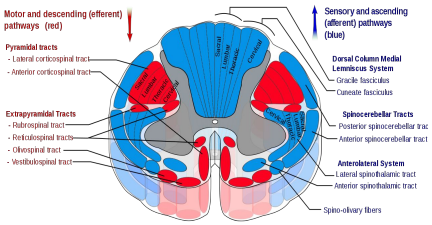
Know that the motor tracts divided into Pyramidal & Extrapyramidal tracts with their tract for each one

Descending Motor System (UMN)

Pyramidal tract

- Corticospinal tract — Supply the opposite side
- Corticobulbar tract, also called corticonuclear



Extrapyramidal tracts

the main function is set posture

- Rubrospinal tract help — Corticospinal but not as good as Corticospinal
- Reticulospinal tracts
- Vestibulospinal tracts — always excitatory
- Tectospinal tract
- Olivspinal tract

Corticospinal (Pyramidal) & corticobulbar Tracts:

Percentage of arising fibres are IMPORTANT to know

Cells of origin:

- 30% originate from the primary motor area (M1) / motor area 4
- 30% from the premotor areas, and supplementary motor areas.
- 40% from the somatic sensory areas/ parietal cortex posterior to the central sulcus.In parietal lobe

مسؤول عن كل الاحاسيس

Corticospinal (Pyramidal) & corticobulbar Tracts:

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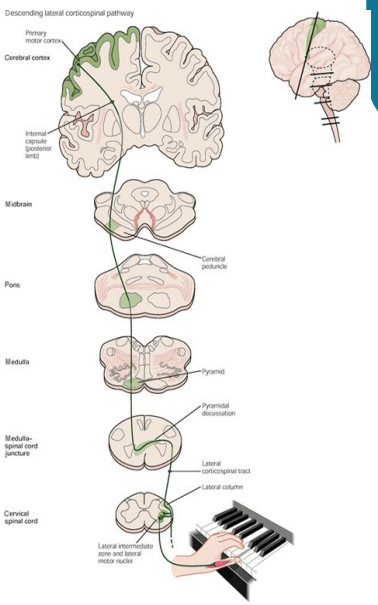
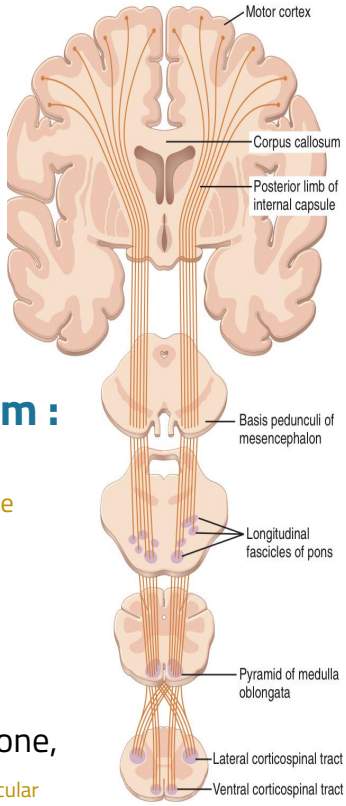
Origin: Sensory Cortex, Primary Motor Cortex, Premotor and supplementary Cortex → Internal Capsule → Cerebral Peduncle (midbrain) → Pons → Medullary Pyramid → Pyramidal Decussation → Lat.Cross & Vent. Uncross White matter in spinal cord → Ant. Horn of spinal cord through a interconnection → α motor neuron of opposite side



Corticospinal Tracts (Pyramidal) Divides into:

	Lateral C.S. Tract	Ventral (anterior) C.S. Tract
Function	These fibers controls and initiates fine discrete skilled movement of distal limb muscles (i.e. Fingers and hands)	These fibers control the axial and proximal limbs muscles so it concern with control of posture.



OtherFunctions of Corticospinal (pyramidal) system :

1-Initiation of fine, discrete, skilled voluntary movements for opposite side

2-Effect on stretch reflex:
Facilitate muscle tone through gamma motor neurons intrafusal fibers

3-Corticobulbar tracts control face & neck muscles & facilitate their tone, and are involved in facial expression, mastication & swallowing.+ Extraocular muscle in eye movement

Rubrospinal Tract :

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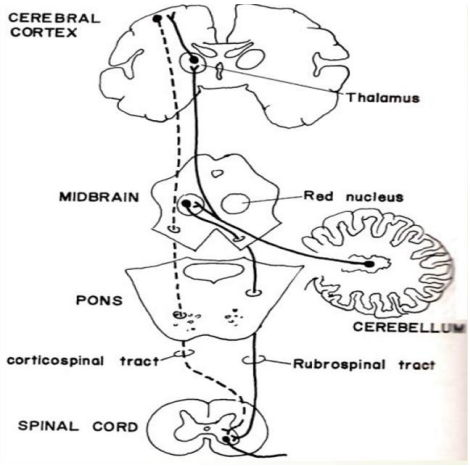
1-It receives **ipsilateral** fibers from the primary motor cortex through the corticorubral tract & from the corticospinal tract .

2-Receive afferents from **contralateral** cerebellum & from basal ganglia .



Function corticorubrospinal Tract :

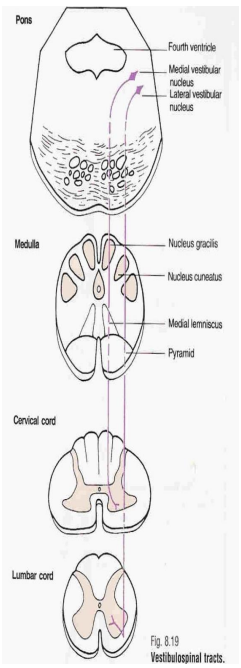
The corticorubrospinal pathway serves as an accessory route for transmission of discrete signals from the motor cortex to the spinal cord.
When the corticospinal fibers are destroyed, discrete fine control of the fingers movements can still occur but impaired.

Rubrospinal tract lies in the lateral columns of the spinal cord, along with the corticospinal tract. Therefore, together are called **the lateral motor system of the cord**,

in contradistinction to a vestibulo-reticulospinal system, which lies mainly medially in the cord and is called **the medial motor system of the cord.**

2- Vestibulospinal (V.S) tracts:

	Lateral V.S. Tract	Medial V.S. Tract
Cells of origin	Lateral V.S Nucleus	Medial V.S Nucleus
Function	Excitatory influences upon extensor motor neurons to maintain posture & righting reflex	Coordination of head and eye movements



Motor tracts

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3- Reticulospinal tracts:

Types	Pontine (Medial) Reticulospinal Tract	Medullary (Lateral) Reticulospinal Tract
Cells of origin	Pontine Reticular Formation which has **high degree of excitability** & they receive strong excitatory signals from the vestibular nuclei and the neocerebellum.	Medullary Reticular Formation
Pathway of the axons	Descends in anterior (ventral) white column at all levels of the spinal cord. Terminates mainly on interneurons in the spinal gray matter.	Descend in lateral white column at all levels of the spinal cord on both sides.
Function	Increases the medially situated Gamma and alpha efferent activity (excitatory to axial & antigravity, extensor muscles of the body (lower limb) & increases muscle tone) -It causes powerful excitation of antigravity muscles - It is excitatory for extensors & inhibitory for flexors (unlike rubro-spinal).	-It receives strong input (afferent) from 1. The corticospinal tract (the premotor area of cerebral cortex) 2. The rubrospinal tract (red nucleus) 3. The paleocerebellum -These activate the medullary reticular inhibitory system to counterbalance the excitatory signals from the pontine reticular system -Synapse with interneurons that inhibits Gamma and Alpha efferent activity of antigravity and extensor muscles, but they facilitate the Gamma and Alpha of flexor muscles. -Transmit inhibitory signals to antigravity extensor muscles & decreases muscle tone. (Like rubro-spinal)

Basically both the Vestibulospinal tracts and the Reticulospinal tracts help to maintain posture. The main differences in achieving that are:

1. The R.S tract is both excitatory and inhibitory, but the V.S is only excitatory.
2. The V.S tract maintains posture by being mainly stimulated by the vestibular apparatus.

R

Physiology of Stretch reflex

Q from females Doctor

What's the type of gamma efferent?

What's the role of gamma efferent?

What's the benefits of gamma efferent?

VERY VERY IMPORTANT Slide

Stretch Reflex
(Myotatic Reflex)

R

Sudden stretch

Lead to sudden contraction

Dynamic Response

sudden change in the length

Sustained stretch
(Slow, maintaining contraction)

Lead to maintained contraction

Static Response

continues stretch

Muscle spindle

Muscle spindle:

Intrafusal fibers.

1-the receptor located inside muscle & detects changes in muscle length (its the sensory receptor)

2. consist of 3-12 small muscle fibers (intrafusal fibers) within the CT capsule.

3-each intrafusal fiber has:
-central **non-contractile** area (receptor)
-peripheral **contractile** area
on each side of central zone, it has actin & myosin.

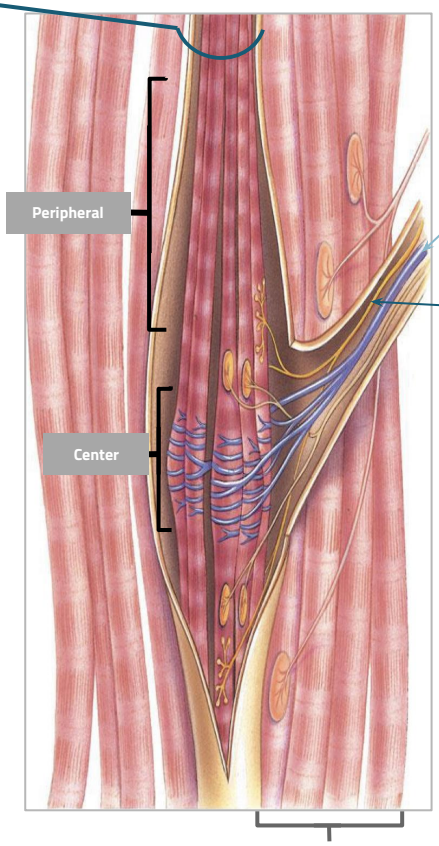
4. There are two types of **intrafusal fibers:**

1-Nuclear **bag** fibers
(2/spindle)*
Central area is dilated with group (bag) of nuclei.

Nuclei
تكون متجمعة
في الوسط

2-Nuclear **chain** fibers
(4+/spindle)

One line of nuclei in a chain in the receptor zone



Extrafusal fibers.
Note that its Not a part of muscle spindle

Overview of innervation
(Afferent, efferent)

1. Primary (Ia)
aka: **annulospiral**
The purple one.

2. Secondary (II)
aka:**flower spray***
The orange one.

2 types of **Afferent** nerves:

The difference between these two afferent is related to the two types of intrafusal fibers, how?

Primary afferent will carry sensation from
1-Nuclear **bag** fibers
2-Nuclear **chain** fibers
whereas the secondary afferent will carry information from:
1-Nuclear **chain** muscle **-only-**

Names of afferent is **important**

Gamma
1-Plate endings
2-Trial ending
→ Intrafusal

Alpha
Alpha motor neurons synapse with the afferent sensory neurones in the spinal cord (secrete glutamate)
→ Extrafusal

Efferent
Motor

Where is the Integrating center?
(spinal cord) AHC
What is the Effect?
Muscle contraction & Reciprocal Inhibition of antagonist

Innervation of the muscle spindle

Afferent (Sensory fibres)

Efferent (Motor fibres)
Next slide.

1- Primary (annulospiral) Ia

-**Fast**,transmits sensory signals to the spinal cord at a velocity of 70 - 120 m/sec
-encircle receptor areas of **nuclear bag fibers** mainly, but also nuclear chain fibres
-17 micrometers diameter
-Discharge most rapidly if the muscle is suddenly stretched(**dynamic response**) & less rapidly (or not)during sustained stretch (static response)
-Measure the rate & or velocity of change in muscle length of nuclear bag fibres

2- Secondary (flower spray) II

-innervate the receptor area of the nuclear chain fibres ONLY
-8 micrometers in diameter
-Discharge throughout the period of muscle stretch, (sustained stretch) measure mainly muscle length (**static response**)
- directly proportional to the degree of stretch

N.B: IMPORTANT

	Supplied by Which afferent	Responsible for
Nuclear bag Fibres	**primary** endings only	the **dynamic response**
Nuclear chain fibres	both **primary** and **secondary** endings	the **static response**

IMPORTANT Slide, especially the important note about γ motorneurons

R

Innervation of the muscle spindle

Afferent (Sensory fibres)
Previous slide

Efferent(Motor fibres)
Gamma (γ) efferent endings terminate on the peripheral contractile parts of the intrafusal muscle fibres

1-Plate endings

End mainly on the nuclear **bag** fibres called (dynamic gamma efferent)

وش دخل Dynamic?
Because it's found in nuclear **bag** fiber
Which have which type of afferent?
Primary
Primary is responsible for which response?
DYNAMIC !
شفينا نهاوش؟

Basis of tendon jerk (knee, biceps, triceps)
Role of Dynamic gamma efferent (plate endings):

-Tapping the tendon, stretch the muscle, so it contracts and shorten,nuclear bag fibres relax during muscle contraction, its sensitivity to stretch decreases تحس بالشد والآن ارتخت أكيد بتقل بالعقل
-Plate gamma endings which end mainly on the nuclear bag fibres periphery, enhances the dynamic response[1]

2-Trail endings

end mainly on nuclear chain fibres called (static gamma efferent)

وش دخل static?
Because it's found in nuclear **chain** fiber
Which have which type of afferent?
Secondary mainly.
Secondary is responsible for which response?
Static
معد هاوشنا

The function of the γ motoneurons (either static or dynamic) is to **regulate the sensitivity** of the intrafusal muscle fibres.
-Activation of γ motoneurons will cause contraction of peripheral parts of the muscle spindle which Increase muscle spindle sensitivity to stretch.
- When γ-d (D donated to dynamic) fibers excite the nuclear bag fibers , the dynamic response of the muscle spindle become enhanced.
- Conversely, stimulation of the γ-s(S donated to static) fibers ,which excite the nuclear chain fibers enhances the static response. [1]

1
انا عارفين إن السنتر ما بنقبض ابدًا فلما نرسل motor effrent نستهدف > periphral
طيب وش الفايدة من الأطراف؟
اذا شدت الاطراف بينشد الوسط بعد، زي الخيط شديه من الطرفين يشتد اوسطه! واذا صار الوسط مشدود وإنا عارفين أنه مليان من Afferent sensory fibers
فكأنه بيحسن عمل السنتر ويصير يعلم الافرنت عن الشد أول بأول
-المكان يحس بالشد، فلازم نخليه على طول مشدود عشان يوصل المعلومات للسبانيل كورد-
reflexبيحسن ال

IMPORTANT

- **Alpha- gamma COACTIVATION: to avoid opposition**

Signals from the motor cortex to the alpha motorneurons, mostly transmitted to the gamma motorneurons simultaneously, an effect called coactivation.
it's the maximum stimulation

- **The purpose of Coactivation:**

First, it keeps the length of the receptor portion of the muscle constant.
Otherwise receptor portion of the spindle would sometimes be flail and sometimes be overstretched, causing unsmooth muscle contractions.
1- central of reception portion of the muscle constant.
2- Oppose sudden changes in muscle length.

Dynamic stretch reflex (dynamic or phasic Response)

Sudden stretch

sudden contraction

This is the basis of Tendon Jerks (dynamic stretch reflexes)

1. Sudden rapid stretch of a muscle
2. Stimulate Nuclear **bag** fibers which respond to velocity of change of receptor length causes synchronous strong burst of excitatory discharges in annulospiral afferents to the alpha motor neuron
   - causes the latter to send strong motor excitatory impulses to extrafusal fibers.
3. Discharge synchronous* strong impulses to the primary ending mainly to the alpha motor neuron *(motor units discharge all together)
4. Motor alpha nerve Causing sudden contraction of muscle extrafusal fibers (jerk movement)
5. Synchronously (jerk movement) followed by relaxation
6. As the muscle shortens (cause it contract), the spindle becomes **lax** and ceases to discharge هو كان يرسل اشارات لما ينشد فلما صار ريلاكس وقف الديشارج
7. no more stimulation of alpha motor neuron
8. no more excitatory impulses from alpha motor neuron to the extrafusal fibers
9. Muscle relax

Static stretch reflex (static Response)

Sustained stretch

Sustained/maintained contraction

1. Maintained stretch of a muscle
2. Stimulates the receptor portion of the nuclear **chain** fibers
3. discharge slowly, both the **primary** and the **secondary** endings are stimulated to the alpha motor neuron to the alpha motor Impulses from muscle spindle travel through spindle afferents (mainly along secondary ending) to alpha motor neuron , stimulating it to produce muscle contraction)
4. contraction of muscle fibers Asynchronously (motor units not discharge all together)
5. Resulting in mild sustained contraction of muscle extrafusal fibers as long as it is stretched

IMPORTANT COMPARISON

Factors that Influence Stretch Reflex
(all act on gamma motor neurons)

Inhibitory	Facilitatory
Supraspinal: I. Cortical (suppressor area 4 & Area 6) II. Basal ganglia III. Red Nucleus IV. Medullary RF (Reticular formation) **V. paleocerebellum**	Supraspinal: I. Cortical (Primary motor area 4) II. Vestibular N (nucleus) III. Pontine RF(reticular formation) (bulboreticular) **IV. Neocerebellum**
Excessive stretch of muscle (golgi tendon reflex)	Anxiety: Gamma motor neuron will be active
Muscle contraction	Noxious painful stimuli طبعًا الألم بيحفز الريفكلس
مساحة فاضية ماعرفنا وش نقولكم فيها, نقولكم بالتوفيق بكم لغة ؟ **French**:Bonne chance. **German**: Viel Glück. **Italian**: In bocca al lupo.	Jendrassik-manuver هذا تكنيك يوصلنا لريفلكس واضح، كيف؟ يقولون للمريض عض على اسنانك مثلًا أو اضغط باصابعك ضد بعض -اي شيء مؤلم شوي الغاية منها نلهي The cortex from inhibitory impulses للمكان اللي قاعدين نختبره ونخليها ترسل مثبطات لألم الأسنان بدل المكان اللي نختبره وبكذا يصير الريفكلس واضح لنا

Comparison Between Stretch & Inverse Reflexes

	Stretch reflex	Inverse stretch reflex
Stimulus	Increased muscle length	Increased muscle tension
Receptor	Muscle spindles	Golgi tendon organs
Afferents	Type Ia & II fibers	Type Ib fibers
Response	Muscle contraction	Muscle relaxation
Synapses	Monosynaptic	Polysynaptic
RECIPROCAL INNERVATION Regulation	Inhibit antagonists through inhibitory interneurons	Excites antagonistic muscles through excitatory interneurons
PHYSIOLOGICAL SIGNIFICANCE	Regulate muscle length	Regulate muscle tension to prevent excessive tension increase & tendon avulsion
CLINICAL ASSESSMENT	Sudden tap of muscle causes brisk contraction muscle jerk	Overstretch of muscle sudden muscle relaxation (lengthening reaction)

R

Physiology of Eye and Refraction

Doctor mentioned a lot of details about this lecture, I have put them all just in case, but the things he mentioned them as IMPORTANT you will find them with red bold color

R

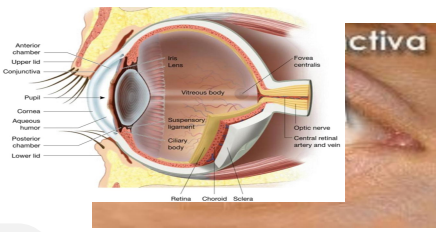
Structure of The Eye

A

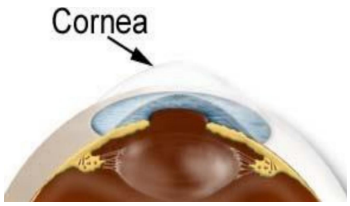
outermost fibrous layer:

protective layer

1. sclera: thick ,white fibrous tissue for protection- spherical appearance.



2. cornea: modified anterior 1/6 of sclera to allow light to enter the eyes. It is transparent and avascular.
   Q. From where it gets its nutrition?
   A. Tears & aqueous humor (Diffusion).



3. conjunctiva: Transparent membrane (epithelium) cover anterior surface of eye, reflected on inner surface of eyelids (lines it and covers the sclera) and Covered with thin film of mucus tears for protection (prevent entrance of microbes and dust), wetness and cleaning.

B middle vascular layer:

1- CONSIST OF:

Iris

Colored part of the eye. Has aperture (pupil) control & allow light to enter the eye. Has the papillary muscles

Pupil

Behind center of cornea, control & allow light to enter the eye,appears black because, as you look through the lens, you see the heavily pigmented back of the eye (choroid and retina) *

Choroids

Inside sclera, highly vascular structure.
Posterior ⅔ of it has retina (the innermost layer lining) not present in the anterior part .
The outermost layer of retina (the photoreceptor) Rods and Cones) depends mostly on diffusion from choroid capillaries for nutrition specially oxygen supply. **

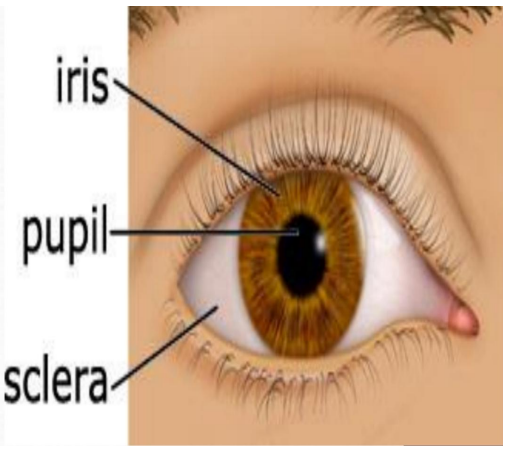
Ciliary body

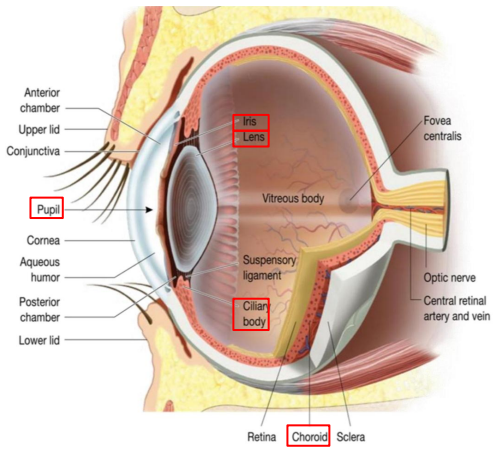
Thick anterior part of choroid consists of Ciliary muscles, Ciliary glands and Suspensory ligaments (zonules) which are attached to the lens.**

Lens

Transparent, biconvex, semisolid. Dioptric (unit of refractive power) power 15-20 D.
held in place by zonule (lens ligament = suspensory ligament) attached to anterior part of ciliary body. Within the cells of the lens, proteins called crystallins are arranged like the layers of an onion, this makes up the refractive media of the lens. Lens helps focus images on the retina to facilitate clear vision.*

❖ Uvea is: choroid + iris + ciliary body fleshy parts in the eye

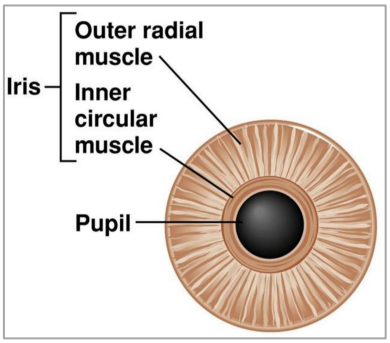




* Girls slides. * Boys slides ** Mixed.

2- **The pupillary muscle** consists of:

1- radial muscle dilates the pupil as in dim light supplied by sympathetic mydriasis
2- constrictor pupillae (circular muscles) constrict the pupil by parasympathetic as in bright light. Myosis



2- **The Anterior & Posterior Cavities:**

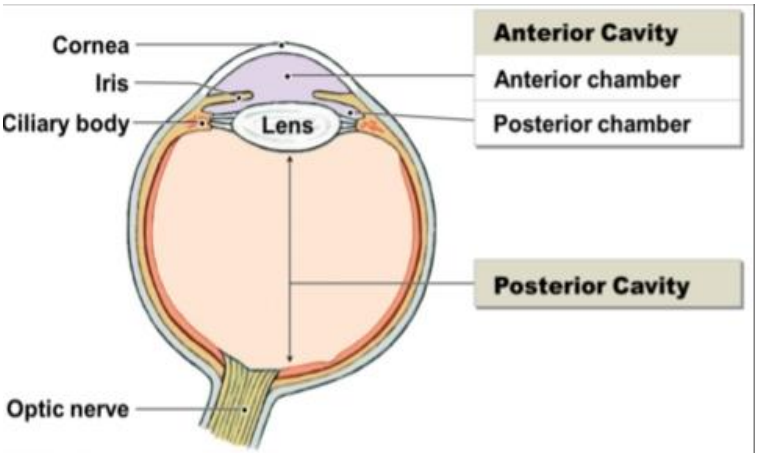
The Ciliary Body (& its suspensory ligament) and lens divide the eye into :

1 Anterior cavity

which contains a fluid called aqueous Humor.
The Iris further divides the anterior cavity into:
a- Anterior Chamber (between cornea and iris).
b- Posterior Chamber (behind the iris; between the iris and lens).

2 Posterior cavity:

which contains fluid called Vitreous Humor.



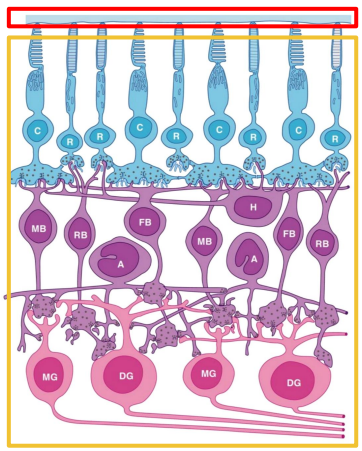
C

innermost layer (retina) Most important layer

R

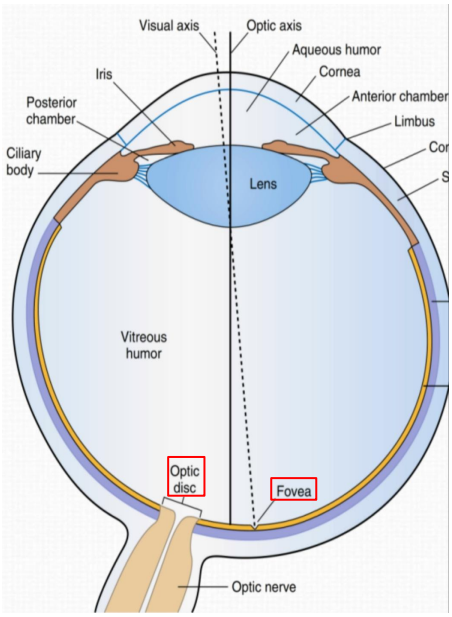
Consists of Outer pigmented part and Inner neural part containing:

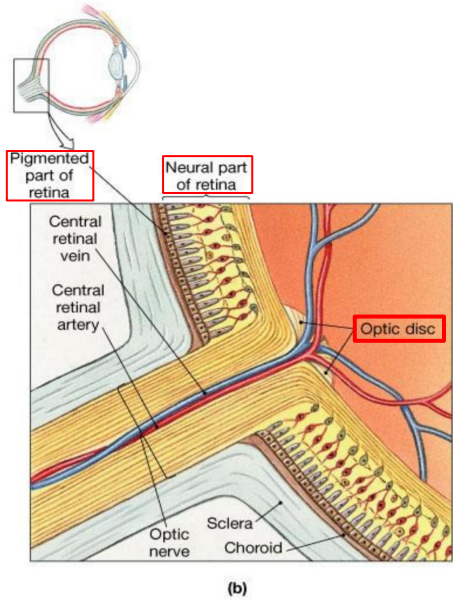
photoreceptors	Called Rodes & Cones. **A) Rods:** are best for vision in dim light (*scotopic vision*). **B) Cones:** are best for vision in daylight or bright light (*photopic vision*), color vision (color perception) & perception of detail (acuity of vision).
optic disc (blind spot)	3mm medial & above post pole of eye where optic nerve & retinal blood vessels enter (NO photoreceptors so it is blind spot). ما تستقبل الضوء + ما نحس فيها لأن عندنا double vision Find **your** blind spot
fovea centralis	Depression or spot at the center of macula lutea (An important part of the retina)* . Yellow pigmented at post pole of eye. Contains only Cones and has the maximum concentration of it*. Consequently, the fovea centralis is the point of maximal visual activity in the retina and high visual activity for colors vision & details detection. When you turn your eye to look at an object, you tend to place its image in the fovea *.

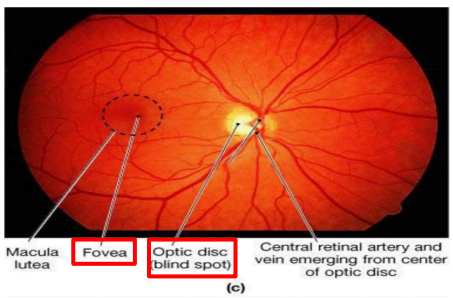


outer pigmented part

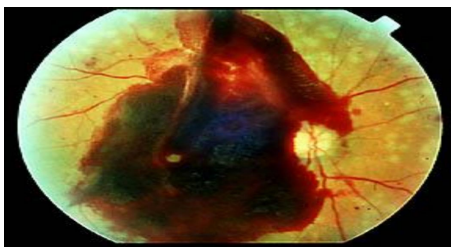
Inner Neural part







Normal ophthalmoscopy view



Retinopathy in diabetes:
Vessels have weak walls causes hemorrhaging and blindness.

Light pathway

R

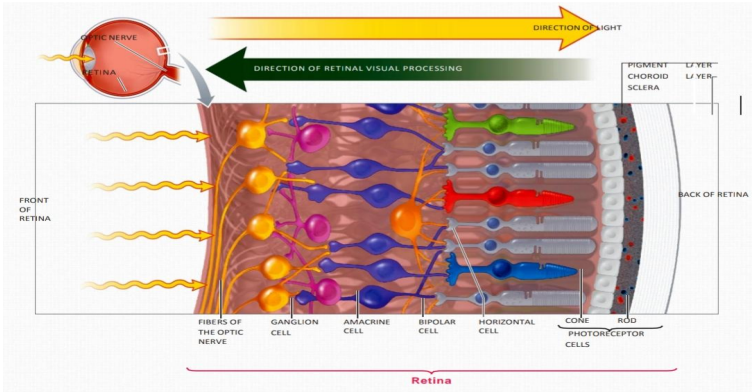
light passes through the lens system of the eye and then through the vitreous humor

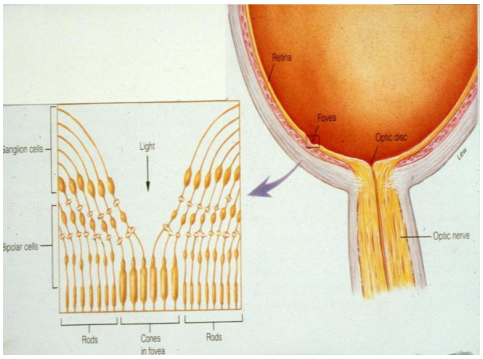
before it finally reaches the layer of rods and cones located on the outer edge of the retina

finally to ganglion cell layer to optic nerve

it enters retina & passes first through the ganglion cells and then through the plexiform and nuclear layers.

Light absorbed by pigment cell layer contain melanin pigment, then to rodes & cons, then impulses pass from them to rest of layers.





Nerve fibers and ganglion axons go two both side away from the center to allow direct striking of the light to the cones of the fovea centralis to give the best color vision and the best details detection

Diopter

Diopters are a measure of refractive power = $\frac{1}{\text{Principle focal distance in } \textbf{meters}}$

Example: If Principal focal distance of a lens is 25cm, how much refractive power would it have?

.

The greater the curvature of the lens the greater the refractive power of the eye (in accommodation, We increase the curvature of the lens)

Concave lenses "neutralize" the refractive power of convex lenses.

Thus, placing a 1-diopter concave lens immediately in front of a 1-diopter convex lens results in a lens system with zero refractive power *

8 Refractive Media of The Eye

R

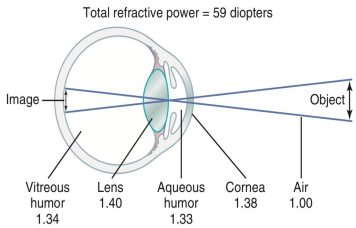
1. The interface between air and the anterior surface of **the cornea,**
2. The interface between the posterior surface of the cornea and **the aqueous humor**,
3. The interface between the aqueous humor and the anterior surface of **the lens of the eye,**
4. The interface between the posterior surface of the lens and **the vitreous humor.**

- a total refractive power of 59 diopters when the lens is accommodated for distant vision.

The Cornea

It's dioptric power is 40-45 diopter at its anterior surface. About two thirds of the 59-60 diopters of refractive power of the eye is provided by the anterior surface of the cornea.

- The principal reason for this is that the refractive index of the cornea is markedly different from that of air
- N.B/ The internal index of air is 1
  - the cornea 1.38
  - the aqueous humor 1.33
  - the crystalline lens 1.40
  - the vitreous humor 1.34

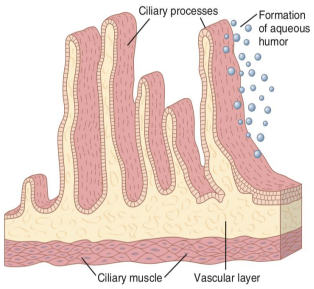


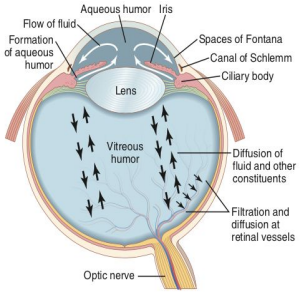
Aqueous Humor

Fluid produced by ciliary body (ciliary processes)>to post chamber > to pupil > to ant chamber > to canal of schlemm at angle of ant chamber > to veins

Function:

- Nourishing avascular structures (cornea ,lens)
- Causes intraocular pressure 10-20mm Hg
- Produced at a rate of 2-3 microliter/min by active transport of NA+, followed by Cl- and HCO3- and then osmosis of water
- Contains many nutrients like amino acids ascorbic acids and glucose
- is **continually being formed** and reabsorbed.
- nourishes the cornea and iris produced in the ciliary body by an active secretion by ciliary processes.
- the aqueous humour is a transparent, slightly gelatinous (gel-like) fluid similar to plasma
- It causes intraocular pressure 10-20 mmhg
- obstruction of this outlet leads to increased intraocular pressure , a critical risk factor for glaucoma



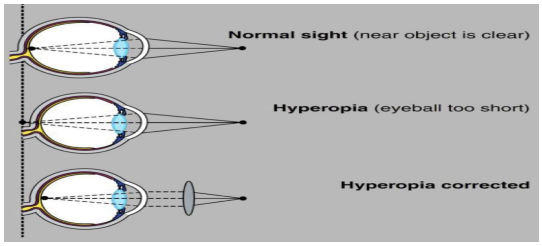
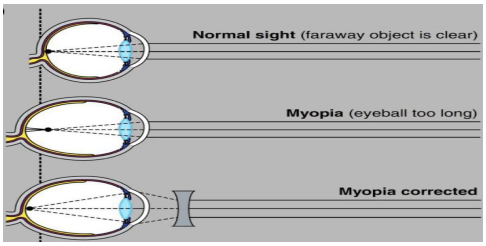


Boys Girls

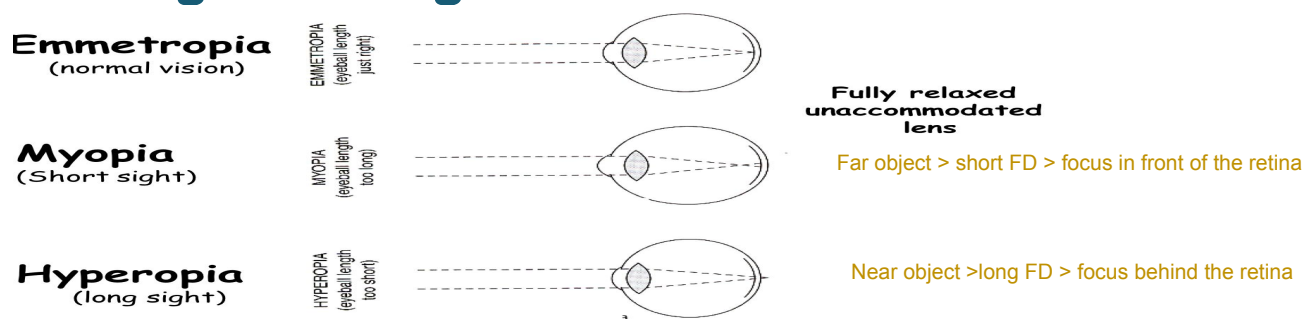
9 Errors of Refraction

R

IMPORTANT

Abnormality	Hypermetropia (hyperopia = far-sightedness)	Myopia(nearsightedness)
cause	**Short (Small) eyeball + weak lens system**	▪ Myopia is thought to be partially genetic in origin However, there is a positive correlation between sleeping in a lighted room before the age of 2 and the subsequent development of myopia. * ▪ In young adults the extensive close work involved in activities such as studying accelerates the development of myopia *
features	An affected individual has to use accommodation even for distant objects. *	Genetic, **large eyeball,**long anteroposterior diameter of the eye,or too much refractive power of lens system or cornea due to its too curved surface
leads to	Continuous accomodation to bring image on retina causes muscular effort on ciliary muscle & prolonged convergence , this leads to headache & blurred vision & finally squint, **focus behind retina**	**focus in front of retina**
Correction by	**correction by biconvex lens.**	**Correction by biconcave lens to diverge rays before strike lens**
graphs		

• Image Focusing

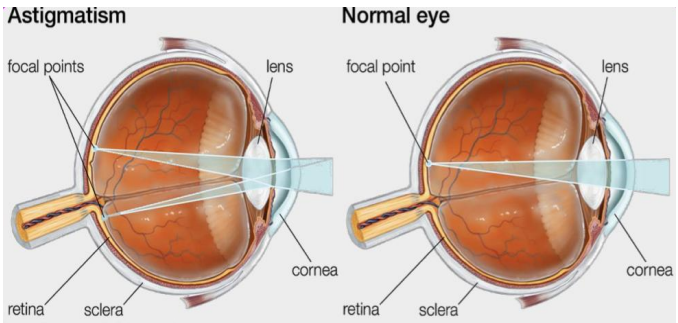


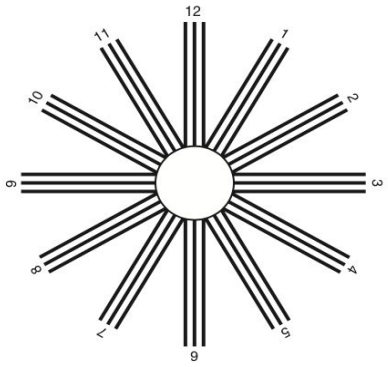
9 Errors of Refraction cont...

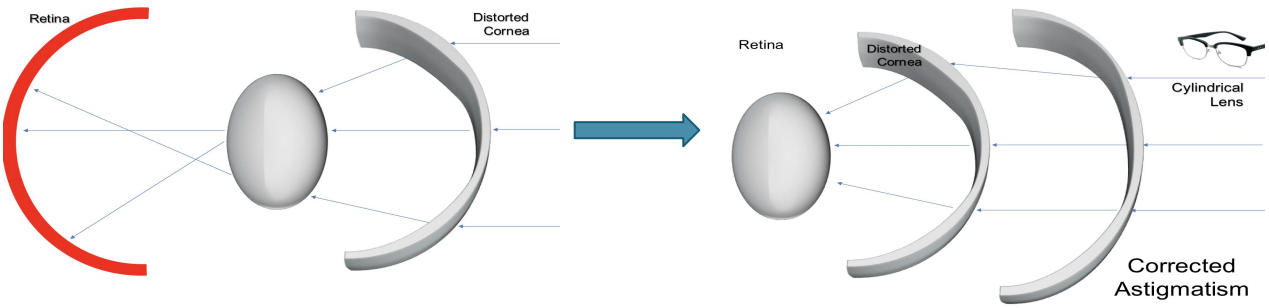
R

Astigmatism اختراف	Presbyopia
❖ **Mainly Uneven & ununiformed corneal curvature, very rare ununiformed lens curvature** ❖ Rays refracted to diff focus > blurred vision ❖ **Correction by cylindrical lens** which bends light rays in only one plane (a focal line)	Eye near point recedes by age due to loss of accommodation > Focus behind retina > correction by **biconvex** lens ciliary للي أعمارهم فوق الخمسين مثلاً يصيرو يلبسو نظارات قراءة لانه يصير لهم muscle weakness

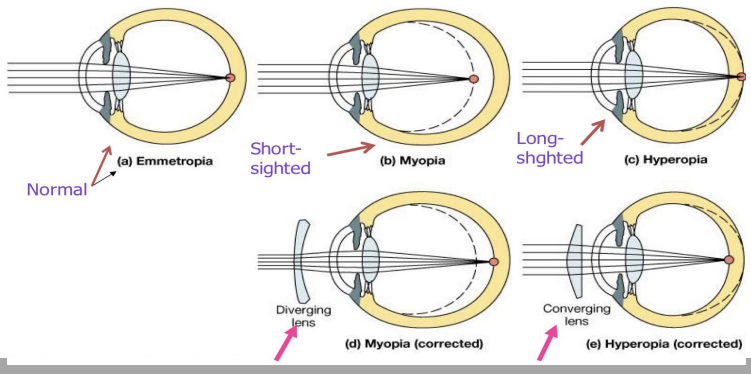
Astigmatism Pictures :

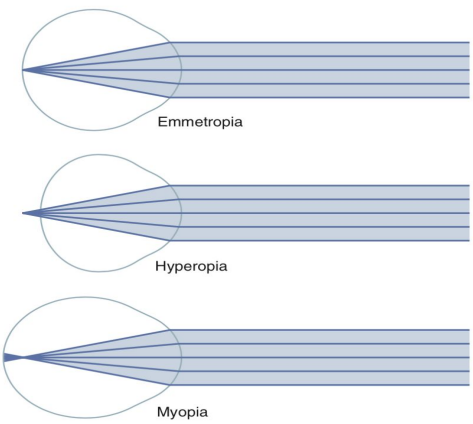






- Visual Abnormalities:





Vision, Accommodation and light Pathway lesions

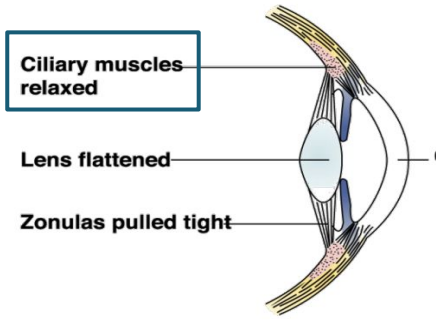
R

Accommodation

Modification of the refractive power of the eye (curvature of the lens)
the goal: clearing the vision view of a nearby object

Distance Vision

1	Ciliary Muscle Relaxed
2	Suspensory Ligaments Under Tension
3	Lens is Flattened
4	Focus on Distant Objects



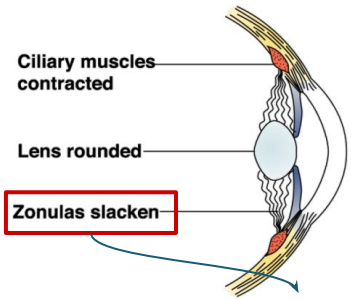
zonulas = Suspensory Ligaments

Accommodation

هذي متى تصير ؟ لما نشوف القريب و لا البعيد؟ القريب. لاننا نخاف ان focus
ترجع ورا، بخلف لا نشوف مكان بعيد الفوكس في مكانها الصحيح "Retina"

1	Ciliary Muscle Contracts
2	NO Tension on Suspensory Ligaments
3	Lens becomes Round (more convex)
4	Focus on Near Objects both circular & longitudinal cilliary muscles contract to pull cilliary

when both of these contract ciliary muscle will move inward and forward



Ciliary muscle become thickened, نزلت وتقدمت

when the two ciliary come close to each other the two suspensory ligament relax lead to curvature of the lens

Slack or Slacken or LAX all of them mean relaxation of suspensory ligament

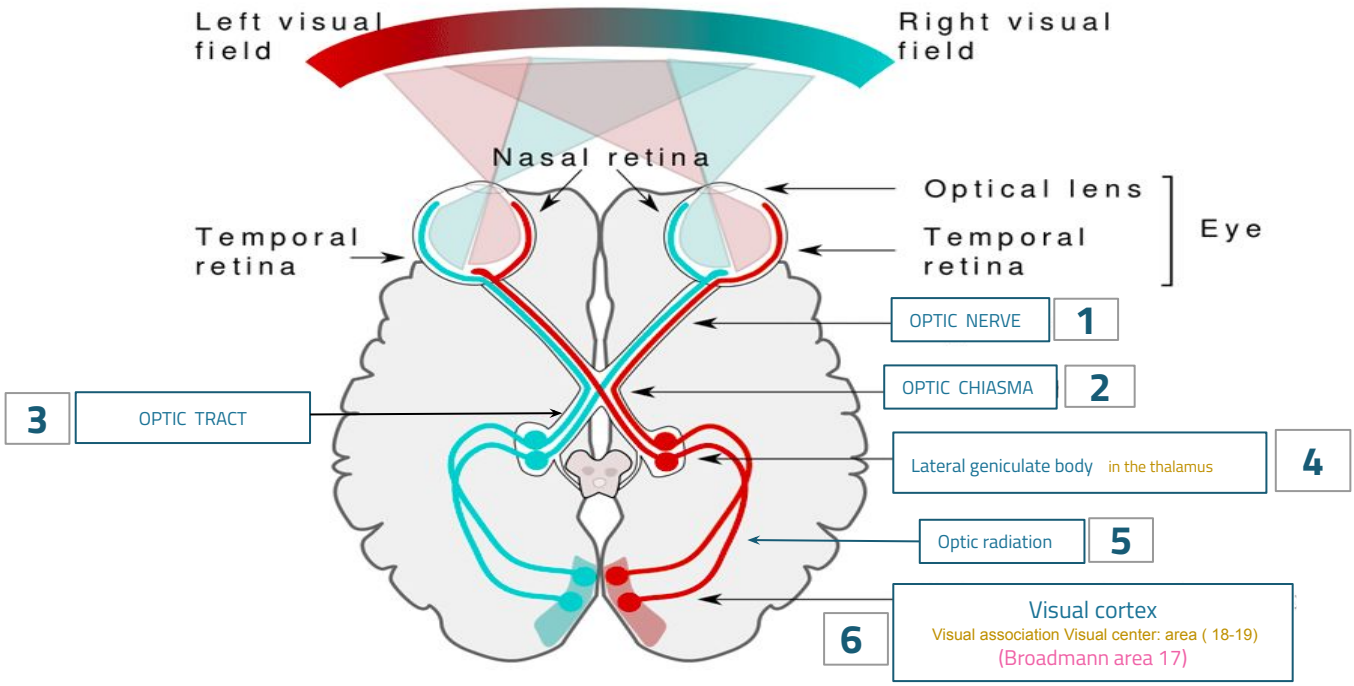
Visual Pathway

VERY IMPORTANT Slide

R

- Pathway from **Retina** to the **Visual Centers** in the Brain
- **Photoreceptors** : Rods and Cones synapse on Bipolar Cells , which in turn , synapse on Ganglion Cells .
- Axons of **Ganglion Cells** constitute the Optic Nerve .
- These axons converge at the Optic disc ,which is also called Blind Spot

  (Why ?) ... Because there are no photoreceptor only way for optic nerve to pass through
- Passing through the Blind Spot they leave the eye , constituting the Optic Nerve



1

Some ganglion cells axons pass from optic tract to pretectal region of midbrain for pupillary reflexes & eye movement

راح midbrain ايضا لكن عشان pretectal nucleus (جنب ال colliculus superior) مسؤولة عن:
(reflex light pupillary) تتوسع العين أو تضيق حسب الضوء زي إذا كان الضوء ضعيف مرة تتوسع عشان تجمع أكثر قدر ممكن من الضوء بعكس لو كان الضوء كثير مرة بتضيق

2

Some axons of ganglion cells from optic chiasma pass directly to hypothalamus for circadian rhythm (light-dark cycle)

النوع الثالث بيروح directly to hypothalamus
مسؤولة عن rhythm circadian
و تخلينا ننام بالليل ونصحى بالنهار

3

Some axons from lateral geniculate body in thalamus to superior colliculus in midbrain to control rapid directional movements of the two eyes and accomodation. R & its miosis component

راح midbrain تحديدًا colliculus superior
مسؤول عن أيش؟
accommodation reflex and miosis of pupil

VISUAL Pathway

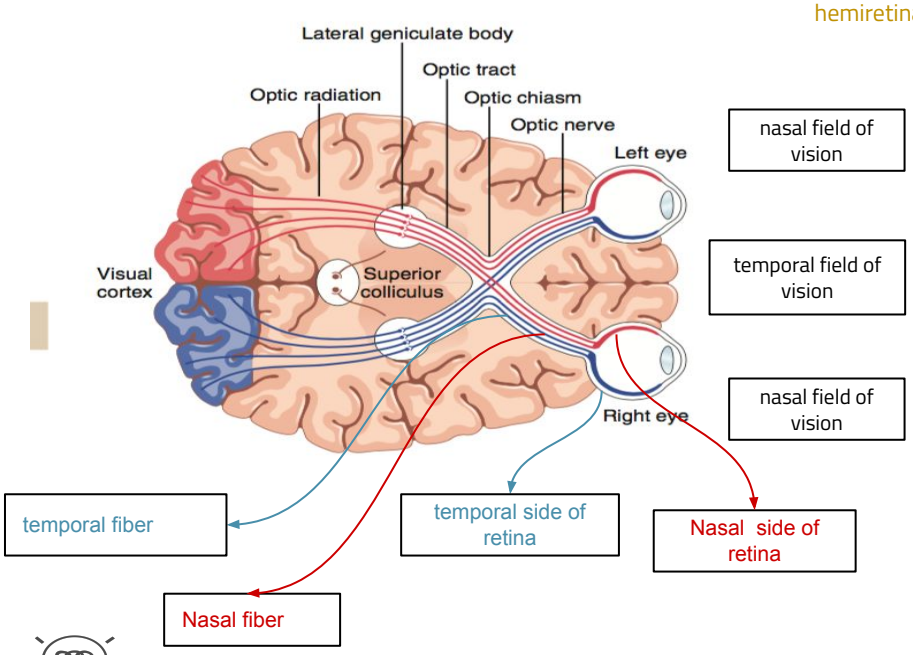
More Explanation for the previous slide

R

- Optic nerve fibers from the medial (nasal) side of retinae decussate **Optic Chiasma**
- Therefore an Optic Chiasma lesion (e,g, Pituitary Tumor) will cause vision loss from the both.. lateral(temporal) halves of the Field of Vision (bitemporal hemianopia)
- Optic nerve fibers from the lateral (temporal) parts of the retinae do not decussate
- Therefore , each optic tract carries fibers from the both the temporal side of the ipsilateral retina + nasal side of the contralateral retina.
- Therefore , a lesion in optic tract will cause loss of vision from the ipsilateral nasal field of vision + contralateral temporal field of vision .

There are two vision fields 1-temporal 2-nasal, the temporal visual field is represented on the nasal hemiretina while the nasal visual field is represented on the temporal hemiretina.
the nasal hemiretina (temporal visual field) decussate in the optic chiasm -> a lesion here can cause loss of the temporal visual field called bitemporal hemianopia (tubal vision), the temporal hemiretina (nasal visual field) doesn't decussate so a lesion in the optic tract can cause problems with both fields called homonymous hemianopia

نسمي المشكلة حسب اللي يشوفه المريض وليس حسب ال hemiretina



Nasal part تطلع منه فايبرز
تشوف الجزء الخارجي
Nasal fibers see the outer portion only.

بالاضافة لو تتبّعون nasal fibers
بتلاحظون هي اللي تسبب crossing فقط

Temporal fibers DON'T involve in decussation

each optic tract carry:
1- Crossed Nasal fiber
2- Uncrossed Temporal fiber

Dr.Faten important Note:
طيب لو صار في chiasm مشكلة؟ خاصة مشاكل pituitary gland
.Because the pituitary gland located beneath the chiasm
> So pituitary tumor for example will cause injury for optic chiasm > cause injury to nasal fibers outer (lateral) part of each field أكيد ماعاد راح ينشاف؟ طيب أي field
(Pts loss half of each eye)

VISUAL PATHWAY & FIELD

Girls slide only.

- The nasal fibers (medial) cross to opposite side at optic chiasma
- The temporal fibers (lateral) do not cross □
- Nasal fibers conveys temporal field (outer)of vision □
- Temporal fibers conveys nasal field (inner)of vision

OPTIC TRACT :

- The left optic tract corresponds to the right ½ of the visual field
- The right optic tract corresponds to the left ½ of the visual field

Pupilary light reflex (استجابة العين للضوء)

R

- Light fall on one eye pupil → constriction of this pupil **(direct pupillary reflex)** and the other pupil **indirect or consensual (**مصاحب للأساسي**)**. when eye (left) is subject to bright light, a direct light reflex occurs (constriction of the pupil) as well as a Consensual (indirect) reflex of the other * Right" pupil.

both eyes respond to the light why?
because 1- the afferent fibers will decussate 2- the efferent (nucleus of edinger westphal) is to both eyes

Pathway of Pupilary light reflex (indirect):- girls slide only

Afferent pathway

Light on eye → Retina → Optic nerve → Optic chiasma → Optic tract → Pass through superior colliculus to end in pretectal nucleus (center of pupilary light refelex)

Efferent pathway

Both oculomotor nerve nuclei (EWN) → Both ciliary ganglia → Supply both eyes by oculomotor nerves → (Short ciliary nerve oculomotor nerves to constrictor pupillae) → Miosis in both eyes

- Conversely, in darkness, the reflex becomes inhibited, which results in dilation of the pupil.

The pupil constricts in response to:

- The accomodation Reflex Its center: superior colliculus
- The light reflex ts center: pretectal nuclus

IMPORTANT

Argyll Robertson pupils (Neurosyphilis) الزهري مرض تناسلي

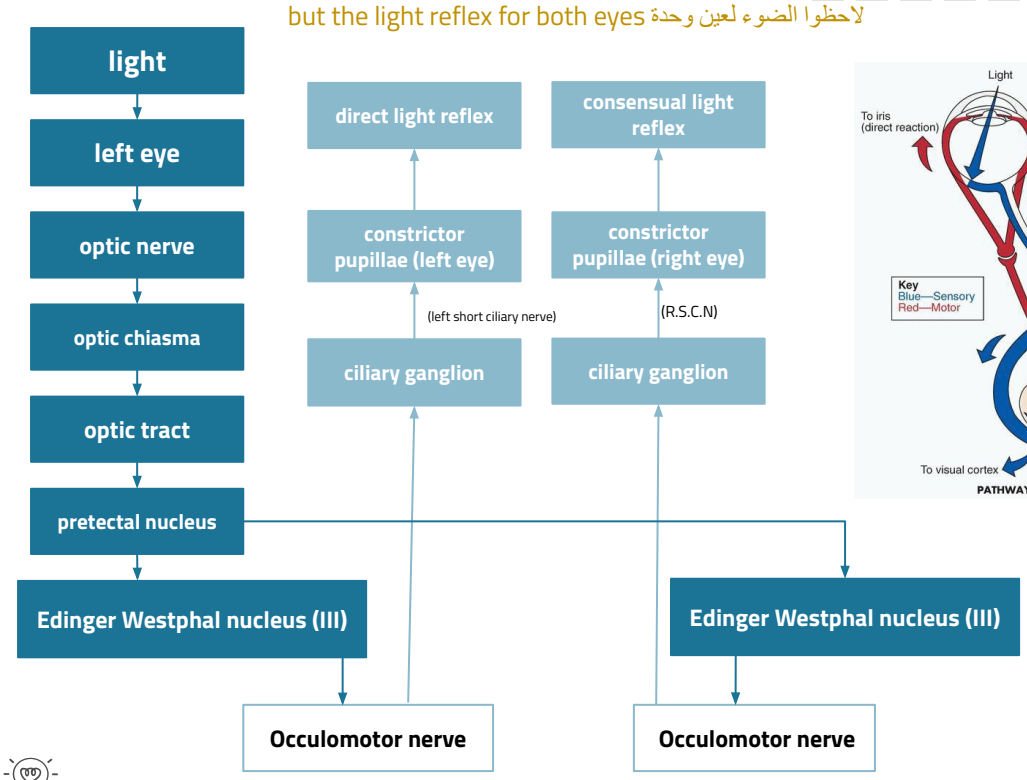
- Pupils constrict in response: to accomodation reflex ,but not to the light reflex
- In syphilis tabes dorsalis which destroy pretectal nucleus only, away from superior colliculus & fibers of accomodation.
- light .R is lost but accomodation R remains can be seen in SLE and DM2 as well

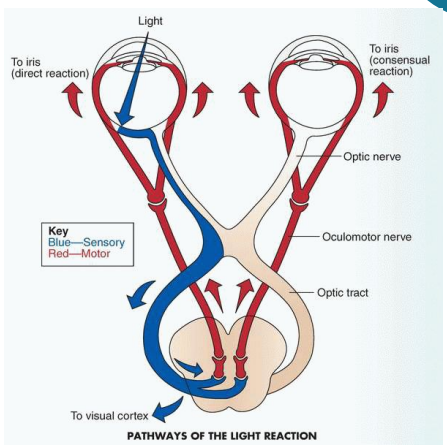
Direct reflex on right & Consensual reflex on left

Girls slide only

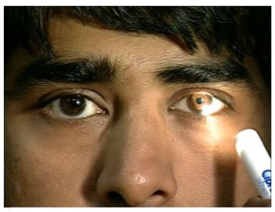
IMPORTANT

but the light reflex for both eyes لاحظوا الضوء لعين وحدة





The light enter on pretectal nucleus and superior colliculus
There is ganglia for motor nerve nuclei and there's ciliary ganglia for motor nerve fiber
then will give occulomotor nerve for both eyes
then will be miosis in the eyes muscles so direct pupillary light reflex for the eye which see
. the light, indierct to the other eye will occur



Three types of retinal ganglion cells and their respective fields

boys doctor said its for your knowledge

1. **W cells:** 40% with small diameter , sensitive or detecting directional movement in the field of vision, and they are probably important for much of our rod vision under dark. تشيل الفايبرز بتاع ال rods اكثر

2. **X Cells:** 55% has a medium size diameter Transmission of the Visual Image and Color Vision
تخدم ال cones اكثر لانها تاخذ اغلب الفايبر منه وهي المسؤولة عن الالوان

3. **Y Cells:** 5% only with large diameter to Transmit Instantaneous & rapid Changes in the Visual Image , either rapid movement or rapid change in light intensity

Phototransduction

IMPORTANT

Photoreceptors

R

Types of Visual Receptors (Photoreceptors)	
Rods	**Cones**
Abundant in the periphery of the retina	Abundant in & around fovea (More central)
Best for low light (dim light) conditions	best for bright light conditions.
see black/white and shades of gray (Monochromatic)	see all colors
100,000,000-120,000,000 rods	5,000,000-6,000,000 cones
Sensitivity to light: • Low Threshold • Sensitive to low intensity light • Night vision	**Sensitivity to light:** • High Threshold • Sensitive to High intensity light • Day vision **Photochemistry of color vision by the cones:**The cones are about 30 to 300 times less sensitive than rods to light
Low acuit	**High acuity**
Color vision: No	**Color vision:** Yes
Dark adaptation: Adapt late	**Dark adaptation:** Adapt early

Shape of Visual Receptors (Photoreceptors) Rods & Cones	
Outer segments	**Inner segments**
Outer segment (modified cilia) has disks full of photosensitive pigment (rhodopsin) react with light to initiate action potential	There is Na-K pump In inner segment
In cones is conical , small and contain 3 types of photosensitive pigments/rhodopsin	Full of mitochondria (source of energy for Na-K pump), it is thick in cones synthesis of the pigment
In rods it is big, rode like and contain one type of rhodopsin	-
There are Na channels in the outer segment (Open and close in response to cGMP)	-
The inner and outer segment are connected by a ciliary stalk through which the photosensitive compound travel from the inner segment (where they are manufactured) to the outer segment of the rods and cones (where they are used)	

Photosensitive Compound (Rhodopsin)

Cones

- In cones rhodopsin (iodopsine) **formed of:**
- Opsin protein (photopsin) + Retinal (also known as retinene1) = aldehyde form of Vit A)
- There are 3 types of rhodopsin/iodopsin in cones (photopsine I,II,III) each respond to a certain wavelength of light for color vision.

Rods

- In rods its rhodopsin **formed of:**
- Scotopsin protein (opsin) + Retinal (also known as retinene1) = aldehyde form of Vit A) = **Visual purple**
- Rhodopsin of the rods most strongly absorbs green-blue light and, therefore, appears reddish-purple
- Rhodopsin forms 90% of rods protein ,stored in disks of rods at outer segment
- **At dark** At dark rhodopsin is in **11 cisretinal form (inactive)** *Activated and degraded in response to light* but light sensitive form which increase sensitivity of rods to light.

Retinal (Retinene) is produced in the retina from Vitamin A, from dietary beta-carotene.

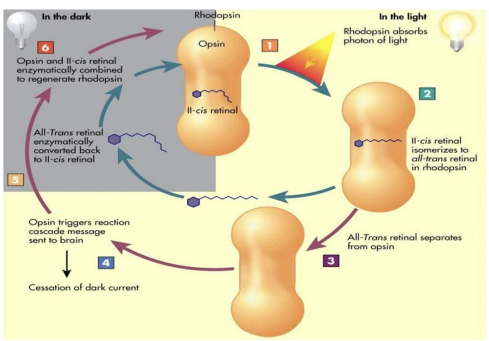
Photoreceptor pigment:

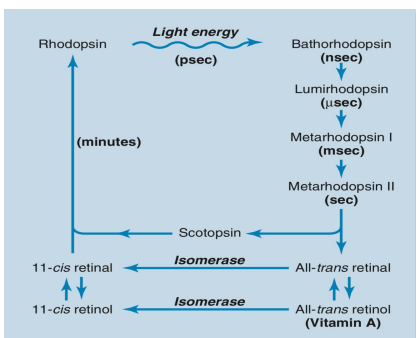
Composition:

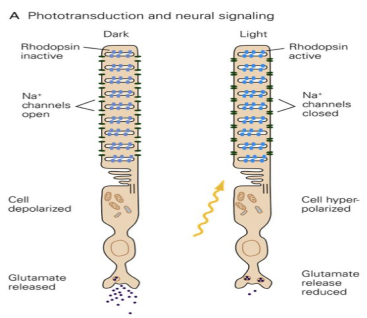
- Retinine1 (Aldehyde of vitamin A) , Same in all pigments
- Opsin (protein), Different amino acid sequence in different pigments
- Rhodopsin (Rod pigment): Retinine + scotopsin

Visual cycle (Bleaching & regulation):

	Light	Dark
In :	**Light** induce Isomerization of 11-cis-retinal into metarhodopsin I then into metarhodopsin II, then into all-trans-retinal (more broken form of metarhodopsin) by a conformational change (bleaching) and all trans-retinal separate from opsin by light and opsin remains alone. Light breaks down rhodopsin.	**In Dark** trans-retinal is enzymatically re-converted to the 11-cis- retinal form via an retinal isomerase enzyme. Since the scotopsin is present alone (having been removed from the rhodopsin) it immediately will combine with 11-cis-retinal to regenerate new rhodopsin. Dark regenerate rhodopsin. **At dark:** 11cis-Retinal in rods + scotopcin → rhodopsin regeneration
cyclic GMP Boys slides only*	In the light, there is a **decrease** in cyclic GMP levels, which closes NA+ channels in the photoreceptor membrane, reduces inward NA+ current, and produces hyperpolarization.	In the dark, there is an **increase** in cyclic in cyclic GMP levels, which produces an NA+ inward current (or "dark current")
The potential recording: Boys slides only*	Hyperpolarization of the photoreceptor membrane decreases the release of glutamate, from the synaptic terminals of the photoreceptor (this creates a negative potential on the inside of the entire cell of about -70 to -80mv)	depolarization of the photoreceptor membrane (the cell remains at about -40mv), which leads to steady release of glutamate at dark
Retinal Visual cycle:	When there is excess retinal in the retina, it is converted in light back into vitamin A, thus reducing the amount of light-sensitive pigment in the retina	The amount of rhodopsin in the receptors varies inversely with the incident light level. (decreases with light) More exposure to light → more Rhodopsin breakdown.







Dark Adaptation:

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- **It means:** increase sensitivity of the photoreceptors when
- vision shifts from bright to dim light
- When a person moves from lighted environment → a dimly lighted environment,
- the retina becomes more sensitive to light & the person will see at dark (accustomed to dark) in about 20 min.(only gross features but no details or colors).
- Rhodopsin in darkness is essential for depolarization of rodes to see in dark & for dark adaptation)
- Reaches max in 20 minutes
- First 5 minutes threshold of cones decrease
- 5 to 20 Sensitivity of rods increase
- **Mechanism of dark adaptation:** increase regeneration of rhodopsin.

Light Adaptation:

When light switch on again, the rodes are knocked out of action (they stop sending AP at high levels of light) & cones start to function to adjust & adapt to the level of brightness in 5 min this is called Light adaptation, it takes less time because here we are breaking the pigments (bleaching) and it takes less time, in dark we are regenerating the pigment which takes more time عملية الهدم تاخذ وقت اقل من عملية البناء

Other mechanisms of light and dark adaptation:

In addition to adaptation caused by changes in concentrations of rhodopsin or colour photochemicals, the eye has two other mechanisms for light and dark adaptation:

1. **A change in pupillary size:**
   This change This change can cause adaptation of approximately 30-fold within a fraction of a second because of changes in the amount of light allowed through the pupillary opening

2. **Neural adaptation:**
   Involving the neurons in the successive stages of the visual chain in the retina itself and in the brain. That is, when light intensity first increases, the signals transmitted by the bipolar cells, horizontal cells, amacrine cells, and ganglion cells are all intense. However, most of these signals decrease rapidly at different stages of transmission in the neural circuit

Nyctalopia: (Night Blindness):

This condition is called night blindness because the amount of light available at night it too little to permit adequate vision in vitamin A-deficient persons.

Vitamine A (main source of retinal of rhodopsin)

Vitamin A deficiency cause rods , cones & retinal degeneration & loss of rods

R/ its not enough to just take dietary Vitamin A so we give Intravenous vit A if receptors are well So it can make rhodopsin before it degenerates completely

Physiology of synapses

Make sure you can differentiate/compare them

Chemical Synapse	Electrical Synapse
Exhibits synaptic delay eg at NMJ reveal a delay of 0.5 to 4.0 mili sec	**Almost no delay in transmission**.
20- to 40-nanometer distance that separates cells **(know that there is distance)**	Cells approach within about 3.8 nm of each other **(Almost no distance)**
Two separate cells that **do not touch**	Gap junctions are intercellular connection that **directly connect the cytoplasm of cells**
Slower than Electrical	**Faster**: many neurons fire synchronously
Mostly **unidirectional**	Mostly **bidirectional**
More **complex behaviors (thinking)**	Are fast, but can produce only **simple behaviors (Sleep arousal)**
Act on receptors which are specific	**Without the need for receptors** to recognize chemical messengers
The response may not be the same as the source.	**The response is always the same sign as the source.**
The response in the postsynaptic neuron is variable. **(speed can increase or decrease)**	Lack Gain the signal in the postsynaptic neuron is the same or smaller than that of the originating neuron **(Speed is almost always constant)**

Factors affecting synaptic transmission:

"this always comes in MCQs"

Changes in internal environment:

- **Alkalosis**: ↑ neuronal excitability ; e.g. overbreathing in epilepsy The overbreathing blows off carbon dioxide and therefore elevates the pH of the blood momentarily Over breathing will cause faint in people with abnormal brain cells
- **Acidosis**: ↓ neuronal activity; e. g. diabetic or uremic acidosis coma
- **Hypoglycemia**: ↓ neuronal activity
- **Hypocalcemia**: ↑ neuronal excitability (tetany) Ca competes with Na to enter the cell, if Ca is low it's easier for Na to enter therefore hypocalcemia increases neuronal activity
- **Hypoxia**: Depression of neurons

Drugs:

- **Caffeine** found in coffee, tea, increases neuronal excitability, by reducing the threshold for excitation of neurons.depolarizes postsynaptic membrane
- **Strychnine**: competes with inhibitory transmitters
- **Theophylline** and **theobromine** increases neuronal excitability, by reducing the threshold for excitation of neurons.
- **Sedatives**, **hypnotics** & **anesthetics**: hyperpolarize (↑threshold) postsynaptic membrane.

Diseases:

- **Tetanus**: Inhibits release of GABA (spastic)
- **Botulism**: Inhibits release of Ach (Flaccid)

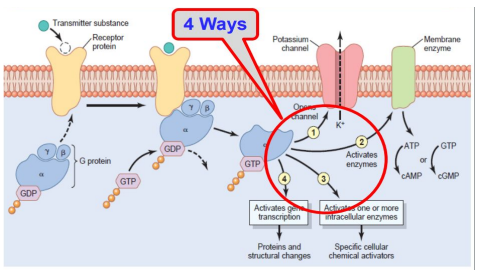
Comparison	
EPSPs	**Action Potentials**
Localized	**All or none**
Graded	**Not localized**
Does not propagate	**Propagate**

EPSPs	IPSPs
1- Opening of Na channels to threshold level (Most Common).	Opening of Cl ion channels through the postsynaptic neuronal membrane.
2. Decrease conduction through Cl or K channels, or both.	2. Increase in conductance of K ions out of the Neuron
3. Various changes in the internal metabolism of the postsynaptic neuron to excite or, in some instances, to Increase excitatory membrane receptors or decrease inhibitory membrane receptors	3. Activation of receptor enzymes that inhibit cellular metabolic functions that increase inhibitory membrane receptors or decrease excitatory membrane receptors.

Fate of Neurotransmitter

After a transmitter substance is released at a synapse, it must be removed by:

1. Diffusion out of synaptic cleft into surrounding fluid.
2. Enzymatic destruction e.g Ach esterase for Ach.
3. Active transport back into presynaptic terminal itself e.g norepinephrine



2nd messenger acts in 4 ways

1- Opening channels
2- Activates membrane enzymes
3- Activates intracellular enzymes
4- Activates gene transcription

Synaptic features

(You should know the details)

One way conduction
Synaptic delay (0.5 ms)
Synaptic inhibition
Convergence and divergence
Fatigue
Summation

Spinal cord functions & reflexes

Classification of reflexes
(according to site of receptor) :

R

A) Deep Reflexes

Know which are Mono/Polysynaptic
Know which are Deep, Superficial, Visceral

BY STIMULATION OF RECEPTORS DEEP IN MUSCLES AND TENDONS

1- *Stretch reflex (tendon jerk)*, they are **monosynaptic** such as knee-jerk (patellar reflex) and ankle jerk . The receptor for all these is the muscle spindle (is located deep within the muscle itself).
2- *Inverse Stretch Reflex (Golgi Tendon organ reflex)* , **polysynaptic** .The receptor is called Golgi Tendon Organ present deep in the muscle tendon
Stretch —>Maintain Muscle Tone in

Also there are
-Extensor Standing/Posture/Stepping ▪ Rhythmic Walking/Scratching

B) Superficial Reflexes

Are **polysynaptic** reflexes . The receptor are **superficial in the skin** or mucous membrane.

Examples are:
- Withdrawal
- Abdominal reflexes and plantar reflex
- Corneal and conjunctival reflexes.
the receptors for the abdominal wall reflex are found on the skin of the anterior abdominal wall

C) Visceral (autonomic)

Are the reflexes where at least one part of the reflex arc is **autonomic nerve**. Stimulation receptors in viscera as micturition, and defecation

Examples are:
- Pupillary reflex
- Carotid sinus reflex

Physiology of brainstem

A sample case

A 58 y/o female patient was referred to you because of recent onset of left **hemiparesis (Corticospinal tract involvement)**, left-sided **loss of proprioception (Dorsal column involvement)** and **right-sided tongue deviation. (Hypoglossal nerve) → Right side means Right side of brainstem**

Integrative functions

You should know what structure is responsible for each function

- It controls consciousness & sleep cycle (alertness and arousal) through reticular formation.
- It has got center for cardiovascular, respiratory & autonomic nervous system.
- It has centers for cough, gag, swallow and vomit.
- Sense of body balance (vestibular function).
- **Substantia Nigra** which is a part of the basal ganglia is present in midbrain and is involved in control of movement.
- Midbrain also contain **red nucleus** which regulate the motor activity through cerebellum.
- Superior and inferior colliculi are situated on the dorsal surface of the midbrain and is involved in visual & auditory processing required for head movements.
- Pain sensitivity control: **Periaqueductal grey matter** of mesencephalon is an area which is rich in endogenous opioid and is important in modulation of painful stimuli.

Origin and function of cranial nerves		
Midbrain	CN 3 (Oculomotor) CN 4 (trochlear)	Eye movement (CN3 constricts the pupils and accommodates)
Pons	CN 5 Trigeminal	Chews, facial sensation
	CN 6 Abducens	Eye movement
	CN 7 Facial	Facial movement, Taste, Salivation
	CN 8 Vestibulchoclear	Hearing, Balance
Medulla	CN 9 Glossopharyngeal	Taste, salivation, Swallowing, Monitors chemo and baroreceptors
	CN 10 Vagus	Taste, Swallow, Lifts palate, Talk, Parasympathetic communication
	CN 11 Accessory	Turns head, Lifts shoulder
	CN 12 Hypoglossal	Moves tongue

Brainstem lesions

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More details in lecture

Midbrain

Pupils:: Mid Position to dilated. Reactivity is sluggish to fixed

Posture:Decorticate

Pons

Pupils:: Pinpoint

Posture:Decerebrate

Medulla

Pupils:: Dilated, Reactivity is Fixed

Fully comatose

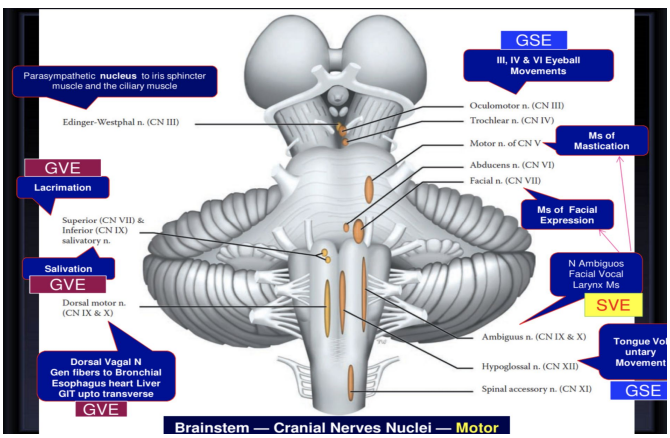
To test brainstem reflexes "these are attractive questions"

- Pupillary and corneal reflexes → CN 3 → Midbrain
- Conjunctival reflex → CN 7 → Pons
- Vestibulo-ocular reflex: Injection of iced water into the ear will produce eyes movement.
- Oculocephalic reflex: Eyes will be fixed when head is moved in or another direction.
- Gag & cough reflexes.
-

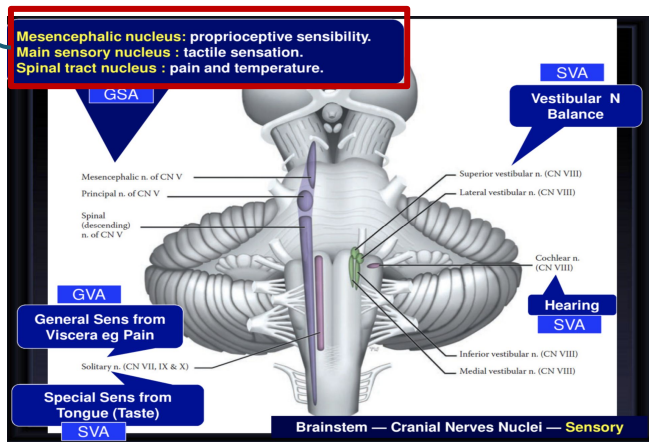
Know the location and the function of nuclei

Trigeminal nuclei, You must know functions of every nucleus
"I like this nuclei" "I would be interested in these ones"

Motor



Sensory



Thank you