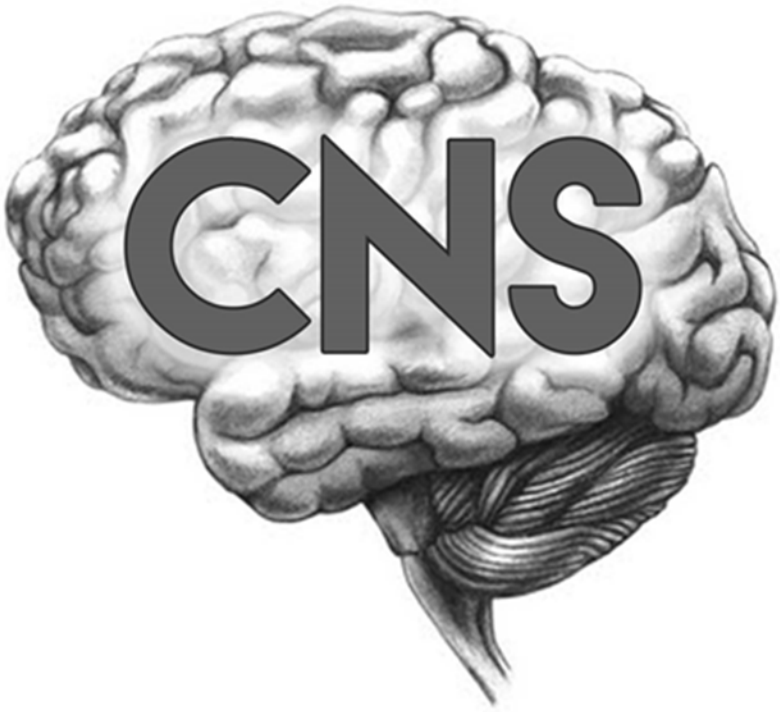

PHYSIOLOGY

✓Sheet ○Slide ○Handout

Number

16

Subject

Neural Retina and Central Neurophysiology of Vision

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Price:

Receptor and Neural Function of the Retina

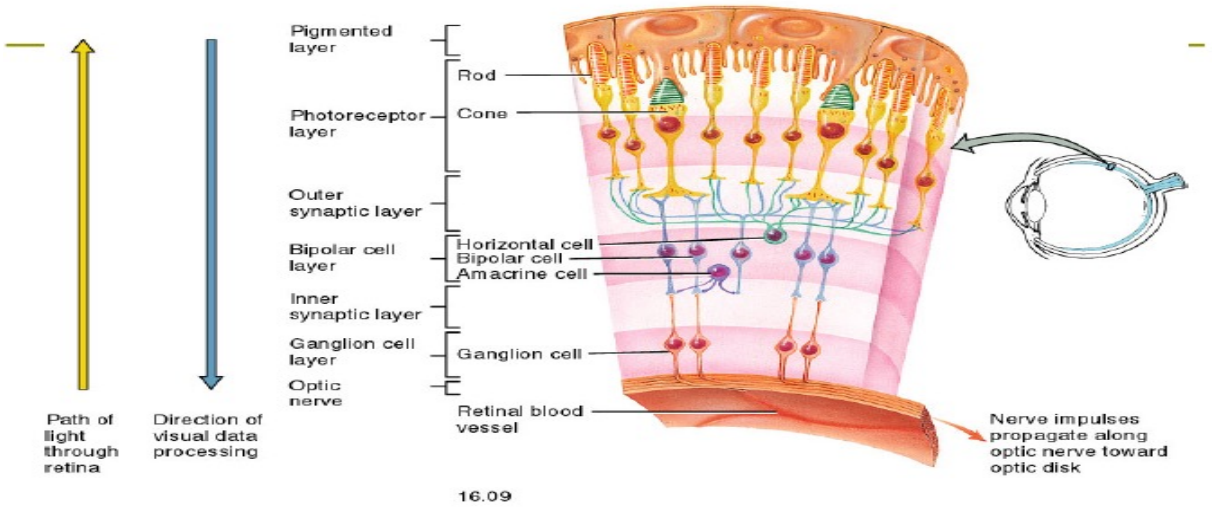
➢ General points/revision of the previous lecture:

- Retinal receptors are of two types: rods, and cones.

- Rods are higher in number (100 million per retina) and are distributed peripherally, meanwhile cones (3 million per retina) are distributed centrally.

- The central fovea, a small area at the centre of the retina, contains only cones.

- The figure below demonstrates the different layers of the retina. The pigmented layer, that is the outermost, is considered part of the choroid by some, and part of the retina by the other. This is of no importance, what matters really is the function. Also worthy of mentioning here, is the fact that the receptors of the visual system are far away from the surface receiving the stimulus (light). This is in contrast to what is common to the other receptor systems.



- Notice, the path of the light and the direction of the impulse are opposite to each other.

- The outer plexiform/outer synaptic layer: this is where the horizontal cells, receptors and bipolar cells synapse. The horizontal neurons are inhibitory interneurons.

- The inner plexiform layer/ inner synaptic: where the bipolar cells synapse with the ganglion cells, and another type of interneurons called the amacrine cells.

- The only cells that send their impulses through **action potentials** are the ganglion cells -and some of the amacrine cells,as for the receptor and bipolar cells they function through electro-tonic conduction, i.e. it generates local and graded potentials. This graded potential allows a response towards a wide range of sensitivities, which is important for discrimination of different light intensities.

- Axons of the ganglion cells form the optic nerve which exits the eye at the optic disc. The area of the optic disc lacks receptors, and is considered as a blind spot.

- In the central part of the retina (fovea centralis), all layers of the retina are pulled aside, to the extent that the cones are exposed directly to the light, that's why if the image occurs at the fovea it is sharp and of great acuity. Also it is in color since the cones are mediating the process.

  - Comparing the rods and cones:

- Rods tend to form more convergences with the ganglion cells than the cones, this is because of the higher number of the rods compared to the cones.

Rods	Cones
high sensitivity; specialized for night vision	lower sensitivity; specialized for day vision
more photopigment	less photopigment
high amplification; single photon detection	less amplification (less divergence 1:1 is more)
saturate in daylight	saturate with intense light
slow response, long integration time	fast response, short integration time
more sensitive to scattered light	more sensitive to direct axial rays

Rods	Cones
low acuity; highly convergent retinal pathways, not present in central fovea	high acuity; less convergent retinal pathways, concentrated in central fovea
achromatic; one type of rod pigment	trichromatic; three types of cones, each with a different pigment that is sensitive to a different part of the visible spectrum, Red, Green and Blue

- <u>The doctor went through the points in the slides above.</u>

- The outer segment of rods and cones has stacks of membranes. Constituting 40% of the membrane component are proteins -mainly rhodopsin-.
  *Rhodopsin found in rods is called ***visual purple***.

- In the synaptic terminal, vesicles of the neurotransmitter are found which, in the visual system, is glutamate. Here, it serves as an inhibitory neurotransmitter.

- Pigment layer: some individuals have genetic deficiencies in melanocyte activity; the resulting deficiency in melanin pigment impairs the function of the pigment layer of the retina which usually contains the melanin. This leads to poor visual acuity due to the scattering of light.

- **Transduction mechanism:**

In the rods and cones we have opsin which is the proteinous part of rhodopsin, and is the part that absorbs the light. Also part of the rhodopsin pigment is the vitamin A derivative; 11-cis-retinal.

In that conformation both the opsin and the derivative are bound to each other. Upon exposure to light, the 11-*cis*-retinal is converted to the *trans* form of the molecule. When this happens, the 11-trans-retinal breaks from the opsin; decomposing the rhodopsin molecule.

In the process of breaking away from the opsin, a number of intermediary compounds are formed. The light-activated form of the rhodopsin (metarhodopsin II), activates a nearby enzyme called *transducin*, which in turn activates c-GMP phosphodiesterase that converts cyclic GMP into a non-cyclic form. This is important because, the c-GMP in the outer segments of the cones and rods stimulates the opening of cGMP-gated Na^+ channels, and when it is decreased these channels close, leading to hyperpolarization. This hyperpolarization results in a decreased release of the inhibitory neurotransmitter. Inhibition is therefore decreased, which means there is excitation.

In the dark, i.e. absence of light, numerous amounts of c-GMP are present at the channels, leading to depolarization of the receptor membrane. (forming an inward current called the ***dark current***)

- Na^+ passes according to its concentration gradient in aim to reach its equilibrium potential which is +60. It does not reach it of course, but as this happens the membrane potential becomes less negative, this depolarization leads to the release of the neurotransmitter; the inhibitory glutamate.

The activated rhodopsin is deactivated, and opsin rejoins the retinal after it has been converted back to the *cis* conformation, and the cycle continues. Rhodopsin kinase mediates the deactivation, and an isomerase catalyzes the retinal conversion.

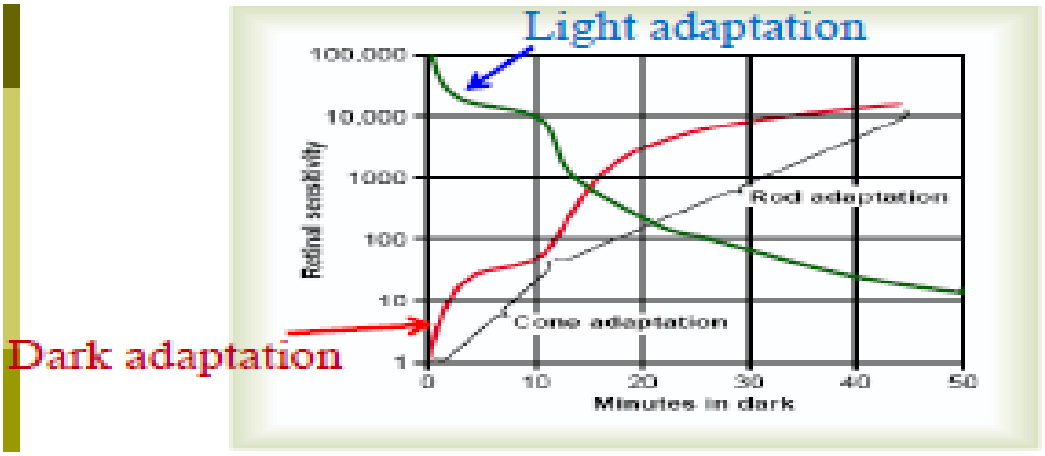
Being high in number and containing too much pigment, the **rods** are the most affected in case of a vitamin A deficiency. If the level of vitamin A begins to decrease, and knowing it is lipid soluble (stored in fatty tissues), a period of 6 months -minimum- of diminished intake is required to develop the deficiency. Decreased formation of rhodopsin, meaning the rods are ineffective, and that is why those individuals are said to have night blindness.

- Vitamin A is found in the pigments of rods and cones and also in the pigmented layer. It is usually stored in the form of retinol (alcohol) but it is converted to retinal through the action of isomerases.

➢ Light and dark adaptation:

Being in a well-lighted area means there is too much light. This light will cause decomposition of the rhodopsin, this in turn will lower the sensitivity of the retina due to the lesser amount of intact pigment. Therefore, the sensitivity is directly proportional to the amount of dye present.

Looking at the figure and starting from time "zero": when you enter a dark room, the sensitivity of the retina begins to increase. First increase is due to the cones; in the first minute there is more generation/reformation of the cones' pigment -as it is mentioned previously cones exhibit faster responses-, this is when the individual begins to view things a little better. Then after 5 minutes, cones pigment has been formed completely, and the regeneration of the rods pigment begins somewhat around that time, but progresses slowly. So, the sensitivity of the retina begins to increase little by little through the regeneration of the pigment by the rods, and continues to reach its maximum (about 100,000-fold increase) around 30-40 minutes later. This applies to what is called as the ***dark adaptation.***



- This is plotted as a logarithmic scale, why is that? This is used to increase the covered range of retinal sensitivity.

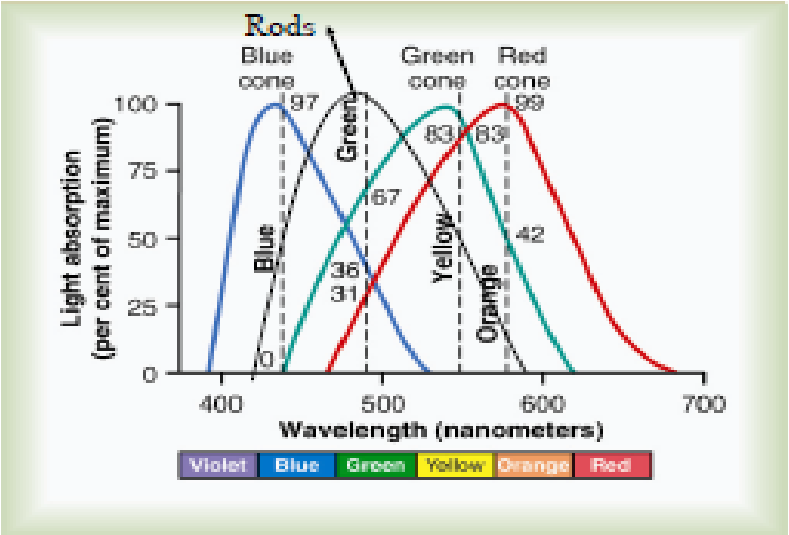
As for the adaptation occurring upon exposure to light -***light adaption***-; the light begins to decompose the pigment. First phase is due to the cones pigment, and then the second phase is due to the decrease in the pigment of rods.

- Another means by which the eye adapts to different light intensities, is through adjusting the size of the pupil; increases the diameter in the dark in order to collect as much light as possible, and decreases the diameter as more and more light is present in the area.

The importance of these adaptations is to continuously adjust the sensitivity of the retina to detect dark and light spots on the image being viewed, as the individual will not be able to detect the image unless the retina discriminates between the dark and light spots on it.

- **<u>Color vision</u>:**

It is mediated through the three different types of cone receptor present; blue, green and red cones. The protein portion -the opsin- in the pigment molecule of the receptor is different in each type, which makes each cone type receptive to a particular wavelength of light. Below you can see the wavelength range of the visible light between 400 and 700 nanometers. Below 400 is the ultraviolet and above 700 is the infrared.



- Approximately and according to the doctor, the blue ranges between 400 and 530, green 430-620, and red 460-700 nm. You can call these the spectral sensitivities of each type.

Now, the way the nervous system interprets color is as follows (follow along with the figure above):

Let's take the color orange, for example. With a wavelength of 580 nm, it lies within the spectral sensitivities of both the red and the green types of cones, but, each receptor absorbs this wavelength to different values; red cones absorb almost 99% of the color wave, while green cones absorb ˜42%, and 0% by the blue cones; a ratio of 99:42:0. The nervous system interprets this ratio as the color orange.

This is how to distinguish between different colors; by stimulating these different cones at different degrees.

- **Color blindness:**

Occurs when a group of color receptive cones is missing. Most common is the green-red color blindness in which one of these two groups is absent –X linked recessive disorder-. Males are affected and females are carriers.

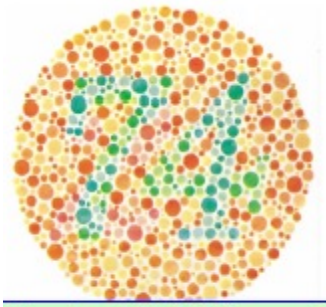
Lack of red cones is known as ***protanopia***, as for the green cones it is called ***deutranopia*** . Only rarely are blue cones missing, and this is usually inherited as <u>autosomal</u> recessive.

The affected individual's perception of the color is different than normal, their nervous system will no longer be able to interpret ratios as it is supposed to, but still, they are able to tell a green color from a

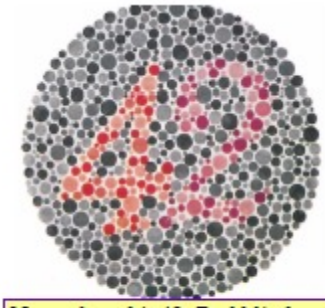
red color when asked to, regardless of how they see it exactly. This is because during childhood they are taught to name colors in such manner. For example when they see a traffic light, they are still able to discriminate between the different colors.

Problem begins to show when the individual tries to pick one of these colors between a mixture of green, red, yellow, and orange. This is difficult for them as it requires a high level of discrimination.

To test for color blindness, Ishihara charts are used˅˅˅



Normal read 74, Red-Green read it 21



Normal read it 42, Red blind read 2, Green blind read it 4

Some charts ask to follow a line rather than to read a number.

- **<u>Neural Organization of the retina</u>:**

As mentioned previously, at the outer plexiform layer there is synapse between the receptors, bipolar cells and horizontal cells. The output of the horizontal cells is always inhibitory to the bipolar cells, mediating the mechanism of lateral inhibition. When the stimulus reaches a certain area of the retina, these cells inhibit the lateral spread of the excitation; forming what is known as an excitatory centre and an inhibitory surround.

-This is essential for the enhancement of visual contrast, forming clear sharp images-

- **Amacrine cells:**

There are about 30 types of amacrine interneurons. Some of them respond at the onset of the light signal, some respond to the movement of the light signal across the retina, and so each type serves different function. Their conduction is through action potentials.

- **Ganglion cells:**

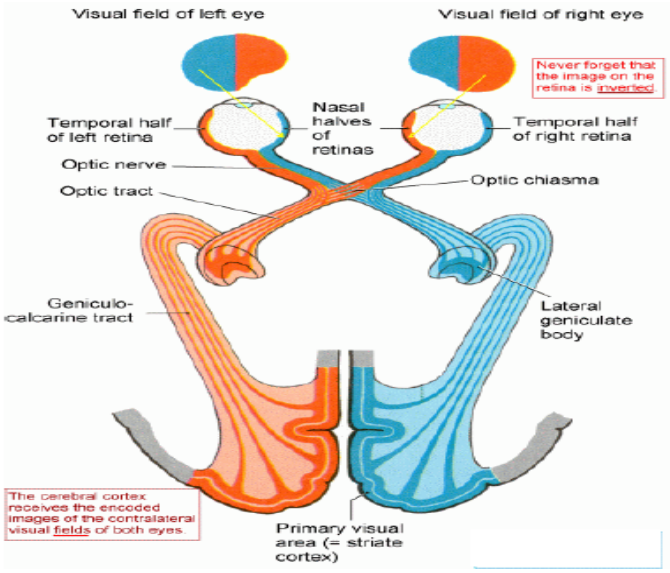
Three types are found: W, X and Y cells. The most dominant are the X cells, having small receptive fields, it is responsible for fine, sharp vision. The smaller the receptive field , the sharper the image.

W cells receive most of the excitation from rods, and are sensitive to directional movement.

Y cells have large receptive fields, and collect from different **total** areas; important to know whether there is light or not. "Respond to instantaneous changes in the visual field."

Central Neurophysiology of Vision

- **Fields of vision**:



In the figure above, notice how each eye has its **visual** field, and each visual field is divided into two; right (nasal) and left (temporal) parts. Also notice the **retinal** fields, which divide into nasal and temporal halves.

Let's take the left eye, for an example. The temporal half of the retina, covers the right aspect of the eye's visual field, and the nasal half of the retina covers the left aspect of the visual field.

As for the right eye, the temporal half covers the left aspect of the visual field, and the nasal half covers the right.

This means that, the **temporal** half of the retina of the **LEFT** eye covers the same aspect, which is the **left**, of the visual fields that is covered by the retinal **nasal** half of the **RIGHT** eye.

Now the cortical representation of the left aspect of vision is present on the right cerebral hemisphere, and the right aspect on the left cerebral hemisphere.

What makes this possible in the visual system, is that the nasal fibers of the optic nerve cross –forming the optic chiasm- to the opposite side, meanwhile the temporal fibers do not and continue on the same side. Behind the chiasm, fibers are now known as the *optic tract.*

- The optic tract on each side is composed of: (1) the temporal fibers of the ipsilateral eye, and (2) the nasal fibers of the contralateral eye. Both of those are transmitting signals from the same side/aspect of the vision.
- Optic chiasm is present superior to the pituitary gland, tumors arising in the gland press on the nasal fibers that are crossing, and the patient represents with what is known as tunnel vision. Common in pediatrics.

- **Retinal projections to sub-cortical regions:**

1. To the suprachiasmatic nucleus of the hypothalamus: this nucleus is concerned with the circadian rhythm of the body, and regulates the secretions of the hypothalamic hormones in terms of timing.
   This is how the visual pathway helps the hypothalamus in distinguishing day from night, and accordingly regulate its hormonal release.

2. To the superior colliculus: this nucleus gives rise to the tectospinal tract, and thus, it coordinates the movement of the head in response to visual stimulation.

3. To the pretectal nuclei: located in the midbrain along with the Edinger-Westphal nucleus of the 3rd cranial nerve. These are involved in the light reflex; sensory input (secondary to light stimulus) is carried by the optic nerve to the pretectal nucleus which in turn sends fibers to the 3rd cranial nerve nucleus that sends efferent fibers with the occulomotor to the constrictor muscle of the iris.

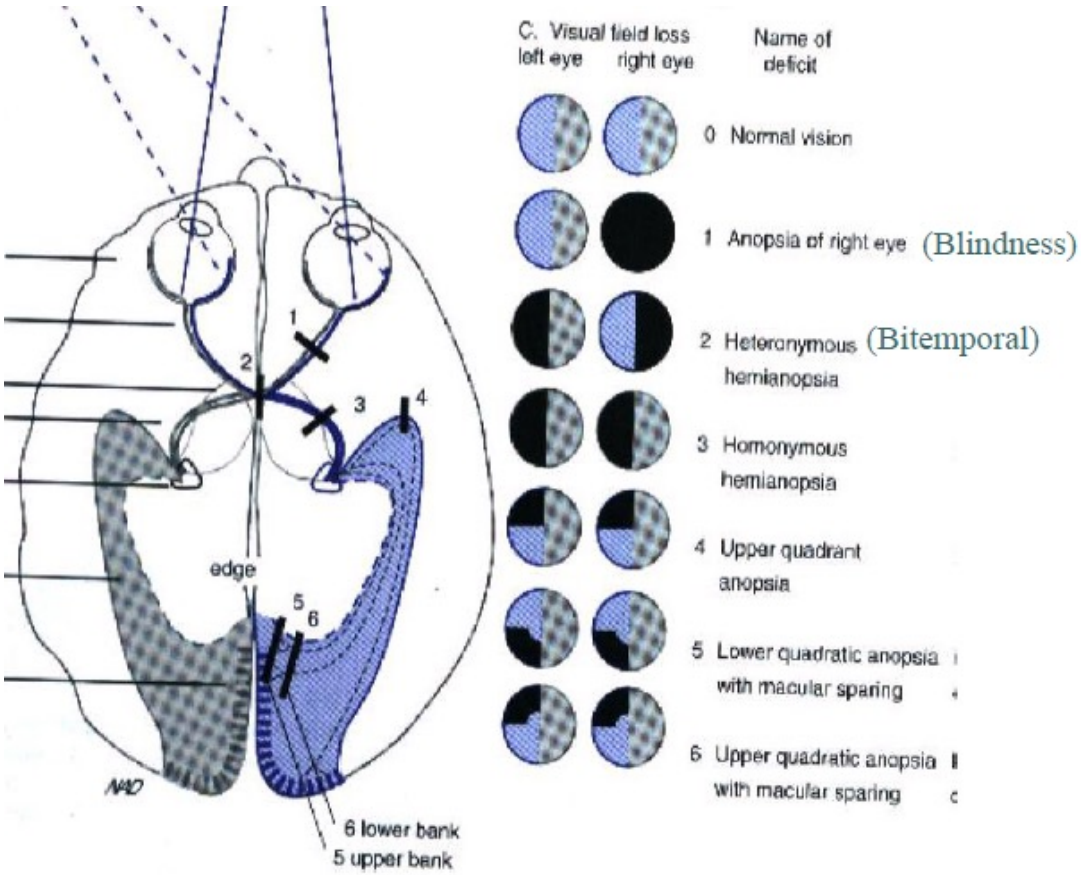
   - The pretectal nucleus sends fibers to the Edinger-Westphal nucleus found on the opposite side as well (fibers that cross). So a stimulation of one eye, leads to the constriction of both pupils, and this is used to test for 2nd and 3rd cranial nerve lesions.
   - Response of ipsilateral eye is called direct light reflex, and the response of the contralateral eye is called indirect/consensual reflex.
   - Loss of both the direct and indirect reflexes occurs in case of an optic nerve lesion. Loss of the direct only - indirect remains functional- means there is a lesion in the occulomotor of the same side.

- **Retinal projection to the cortex:**

Fibers of the optic tract synapse at the lateral geniculate body in the thalamus, which functions as gate to the primary visual cortex. The LGB *optic radiation* projects to the occipital lobe where the visual cortex is.

As it is commonly known, the area of the cortical representation is proportional to the number of receptors. In the visual system, the macula –region for highest visual acuity- is represented with a very large area in the visual cortex. This is why loss of macular vision is much less common than the loss of other forms of vision.

- **<u>Lesions of the visual pathway</u>**:



- Lesion in the optic nerve (1) results in complete anopsia (blindness) of one eye.
- Lesion in the optic chiasm (2) results in bitemporal heteronymous hemianopsia.
- Lesion in the optic tract (3) leads to homonymous hemianopsia; loss of the same side of visual field from both eyes.
- Lesions in the optic radiation: a] if in the upper bank fibers it leads to lower quadrant anopsia, and b] in the lower bank fibers leads to upper quadrant anopsia. Both spare the macula due to its large representative area in the cortex.