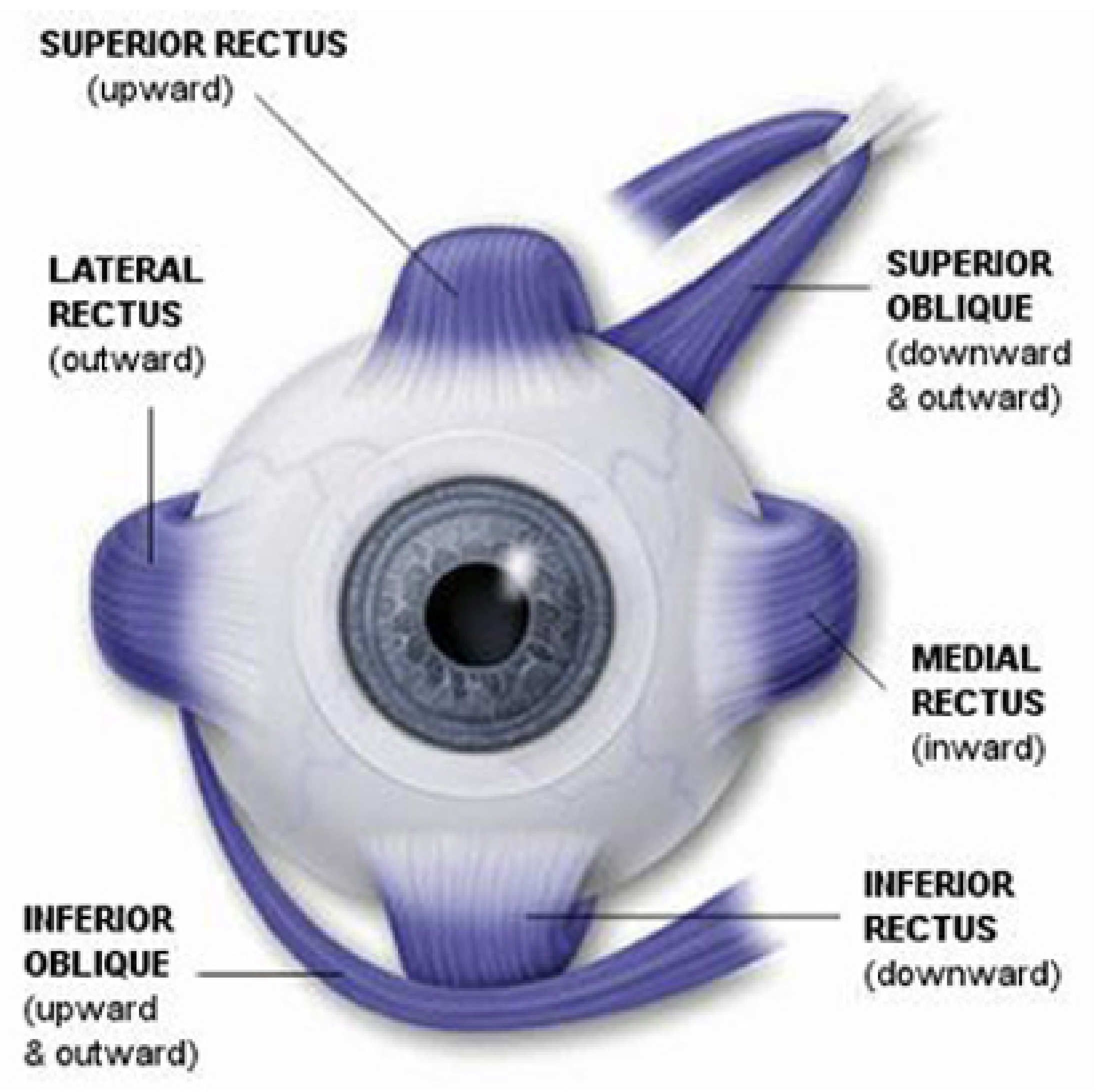
Sensory System & Visual System



Geri Orth
Mendy Varney

First Edition, 2012

ISBN 978-81-323-1433-2

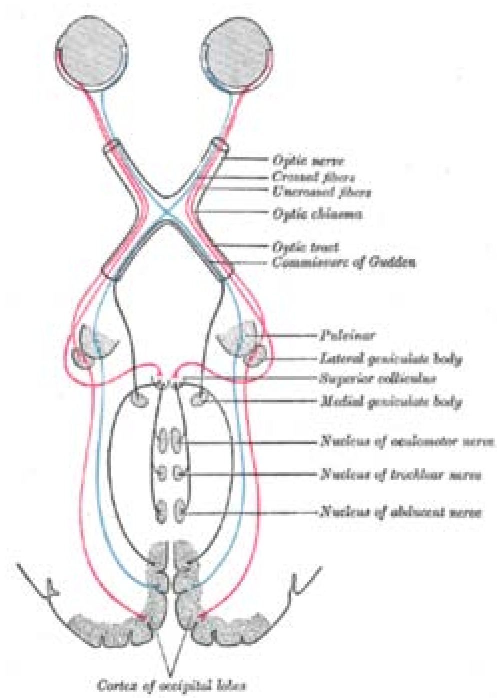
Published by:
College Publishing House
4735/22 Prakashdeep Bldg,
Ansari Road, Darya Ganj,
Delhi - 110002
Email: info@wtbooks.com

Table of Contents

Chapter 1

Sensory System

Sensory system



Typical sensory system: the **visual system**, illustrated by the classic Gray's FIG. 722– This scheme shows the flow of information from the eyes to the central connections of the optic nerves and optic tracts, to the visual cortex. Area **V1** is the region of the brain which is engaged in **vision**.

Latin	*organa sensuum*

A **sensory system** is a part of the nervous system responsible for processing sensory information. A sensory system consists of sensory receptors, neural pathways, and parts of the brain involved in sensory perception. Commonly recognized sensory systems are those for vision, hearing, somatic sensation (touch), taste and olfaction (smell). In short, senses are transducers from the physical world to the realm of the mind.

The receptive field is the specific part of the world to which a receptor organ and receptor cells respond. For instance, the part of the world an eye can see, is its receptive field; the light that each rod or cone can see, is its receptive field. Receptive fields have been identified for the visual system, auditory system and somatosensory system, so far.

Stimulus

Sensory systems code for four aspects of a stimulus; type (modality), intensity, location, and duration. Arrival time of a sound pulse and phase differences of continuous sound are used for localization of sound sources. Certain receptors are sensitive to certain types of stimuli (for example, different mechanoreceptors respond best to different kinds of touch stimuli, like sharp or blunt objects). Receptors send impulses in certain patterns to send information about the intensity of a stimulus (for example, how loud a sound is). The location of the receptor that is stimulated gives the brain information about the location of the stimulus (for example, stimulating a mechanoreceptor in a finger will send information to the brain about that finger). The duration of the stimulus (how long it lasts) is conveyed by firing patterns of receptors.

Modality

A stimulus modality (sensory modality) is a type of physical phenomenon that can be sensed. Examples are temperature, taste, sound, and pressure. The type of sensory receptor activated by a stimulus plays the primary role in coding the stimulus modality.

In the memory-prediction framework, Jeff Hawkins mentions a correspondence between the six layers of the cerebral cortex and the six layers of the optic tract of the visual system. The visual cortex has areas labelled V1, V2, V3, V4, V5, MT, IT, etc. Thus Area V1 mentioned below, is meant to signify only one class of cells in the brain, for which there can be many other cells which are also engaged in vision.

Hawkins lays out a scheme for the analogous modalities of the sensory system. Note that there can be many types of senses, some not mentioned here. In particular, for humans, there will be cells which can be labelled as belonging to V1, V2 A1, A2, etc.:

V1 (vision)

The human eye is the first element of a **sensory system**: in this case, vision, for the visual system.

Visual Area 1, or V1, is used for vision, via the visual system to the primary visual cortex.

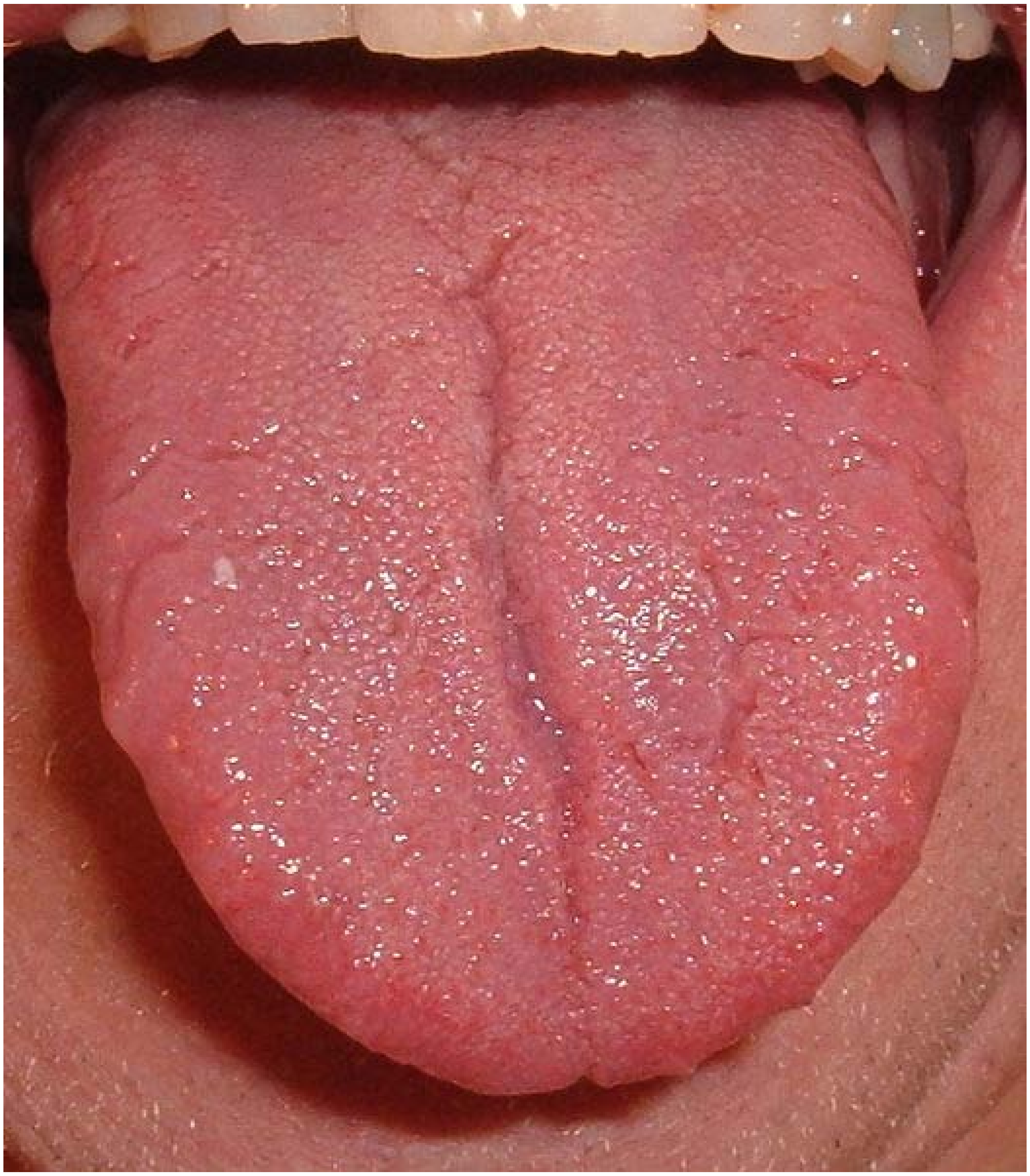
Ear

A1 (auditory - hearing)

Auditory Area 1, or A1, is for hearing, via the auditory system, the primary auditory cortex.

S1 (somatosensory - touch and proprioception)

Somatosensory Area 1, or S1, is for touch and proprioception in the somatosensory system. The somatosensory system feeds the Brodmann Areas 3, 1 and 2 of the primary somatosensory cortex. But there are also pathways for proprioception (via the cerebellum), and motor control (via Brodmann area 4).



Tongue

G1 (gustatory - taste)

Gustatory Area 1, or G1, is used for taste.

O1 (olfactory - smell)

Olfactory Area 1, or O1, is used for smell. In contrast to vision and hearing, the olfactory bulbs are not cross-hemispheric; the right bulb connects to the right hemisphere and the left bulb connects to the left hemisphere.

Human sensory system

The Human sensory system consists of the following sub-systems:

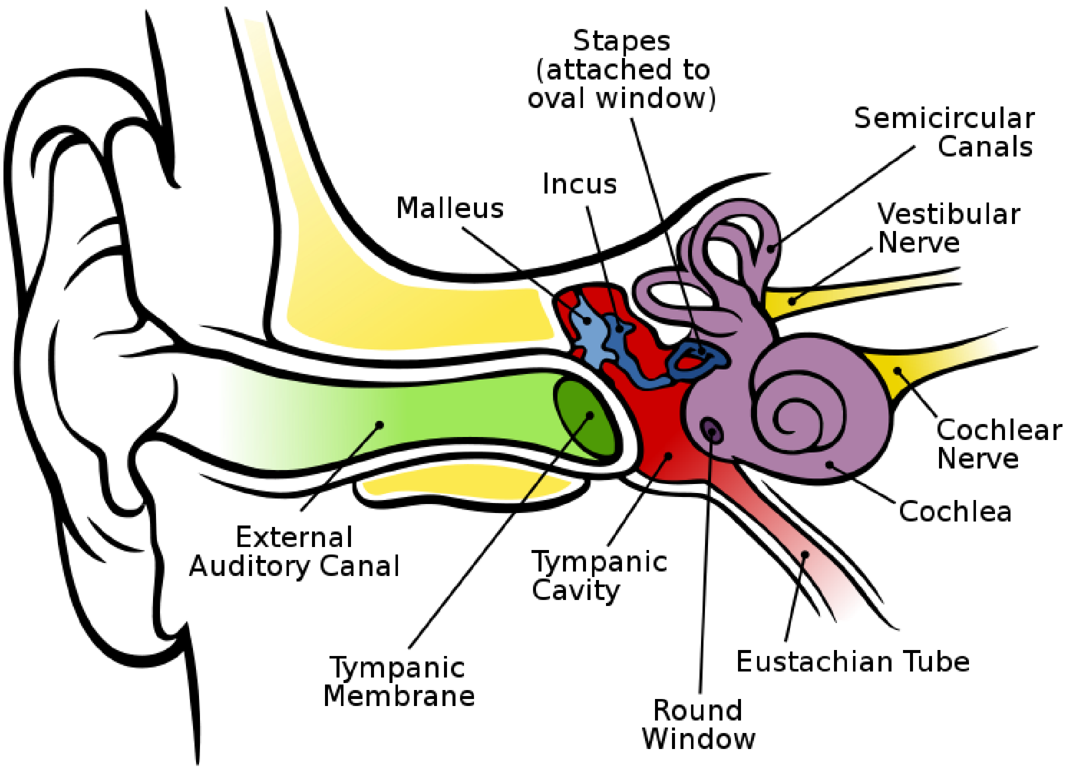
- Visual system consists of the photoreceptor cells, optic nerve, and V1.
- Auditory system
- Somatosensory system consists of the receptors, transmitters (pathways) leading to S1, and S1 that experiences the sensations labelled as touch or pressure, temperature (warm or cold), pain (including itch and tickle), and the sensations of muscle movement and joint position including posture, movement, and facial expression (collectively also called proprioception).
- Gustatory system
- Olfactory system

Human sensory receptors are:

- Chemosensor
- Mechanoreceptor
- Nociceptor
- Photoreceptor
- Thermoreceptor

Chapter 2

Auditory System



Anatomy of the human ear. (The length of the auditory canal is exaggerated in this image)

The **auditory system** is the sensory system for the sense of hearing.

Outer ear

The folds of cartilage surrounding the ear canal are called the pinna. Sound waves are reflected and attenuated when they hit the pinna, and these changes provide additional information that will help the brain determine the direction from which the sounds came.

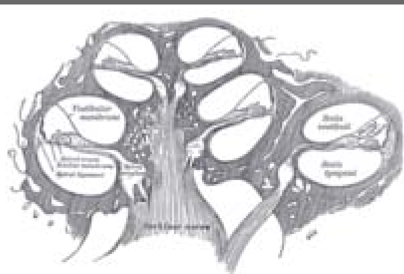
The sound waves enter the auditory canal, a deceptively simple tube. The ear canal amplifies sounds that are between 3 and 12 kHz. At the far end of the ear canal is the eardrum (or tympanic membrane), which marks the beginning of the middle ear.

Middle ear

Sound waves traveling through the ear canal will hit the tympanic membrane, or eardrum. This wave information travels across the air-filled middle ear cavity via a series of delicate bones: the malleus (hammer), incus (anvil) and stapes (stirrup). These ossicles act as a lever and a teletype, converting the lower-pressure eardrum sound vibrations into higher-pressure sound vibrations at another, smaller membrane called the oval (or elliptical) window. The malleus articulates with the tympanic membrane via the manubrium, where the stapes articulates with the oval window via its footplate. Higher pressure is necessary because the inner ear beyond the oval window contains liquid rather than air. The sound is not amplified uniformly across the ossicular chain. The stapedius reflex of the middle ear muscles helps protect the inner ear from damage. The middle ear still contains the sound information in wave form; it is converted to nerve impulses in the cochlea.

Inner ear

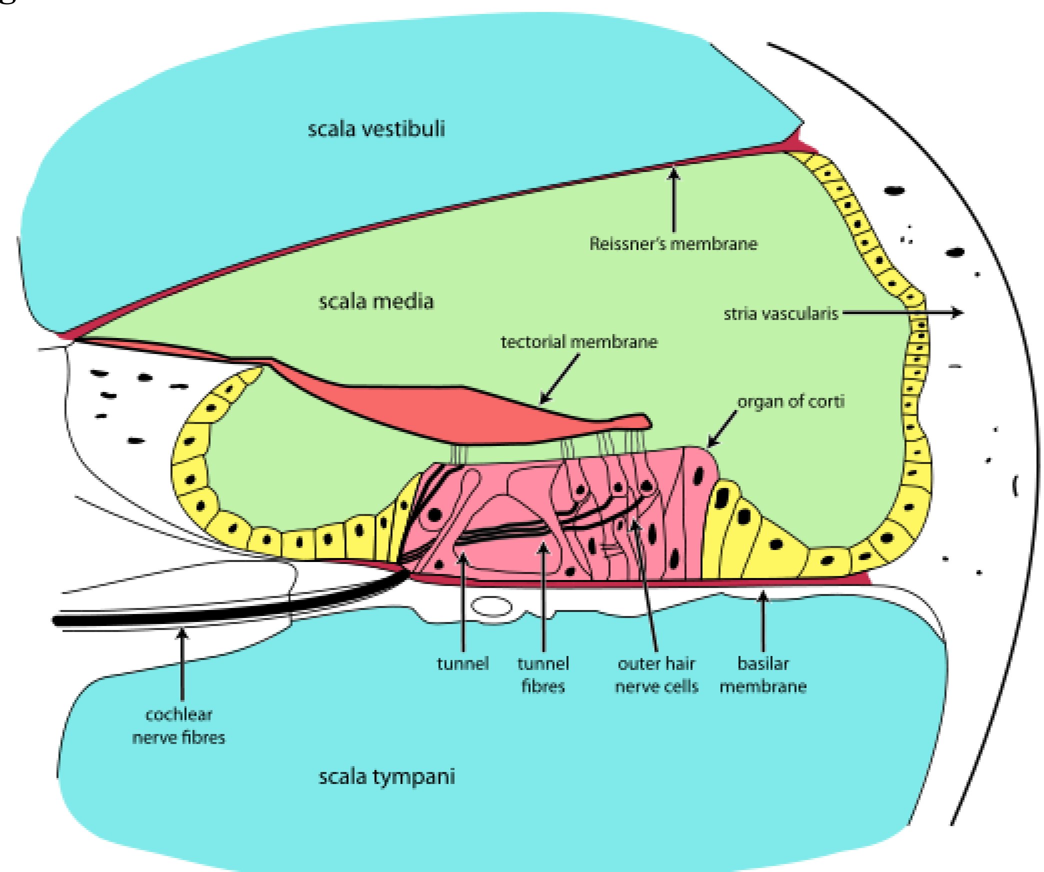
Cochlea



Diagrammatic longitudinal section of the cochlea. Scala media is labeled as *ductus cochlearis* at right.

The inner ear consists of the cochlea and several non-auditory structures. The cochlea has three fluid-filled sections, and supports a fluid wave driven by pressure across the basilar membrane separating two of the sections. Strikingly, one section, called the cochlear duct or *scala media,* contains an extracellular fluid similar in composition to endolymph, which is usually found inside of cells. The organ of Corti is located at this duct, and transforms mechanical waves to electric signals in neurons. The other two sections are known as the *scala tympani* and the *scala vestibuli*; these are located within the bony labyrinth, which is filled with fluid called perilymph. The chemical difference between the two fluids (endolymph & perilymph) is important for the function of the inner ear due to electrical potential differences between potassium and calcium ions.

Organ of Corti



The organ of Corti located at the *scala media*

The organ of Corti forms a ribbon of sensory epithelium which runs lengthwise down the cochlea's entire *scala media*. Its hair cells transform the fluid waves into nerve signals. The journey of countless nerves begins with this first step; from here, further processing leads to a panoply of auditory reactions and sensations.

Hair cell

Hair cells are columnar cells, each with a bundle of 100-200 specialized cilia at the top, for which they are named, which are the mechanosensors for hearing. Lightly resting atop the longest cilia is the tectorial membrane, which moves back and forth with each cycle of sound, tilting the cilia, which is what elicits the hair cells' electrical responses.

Hair cells, like the photoreceptor cells of the eye, show a graded response, instead of the spikes typical of other neurons. These graded potentials are not bound by the "all or none" properties of an action potential.

At this point, one may ask how such a wiggle of a hair bundle triggers a difference in membrane potential. The current model is that cilia are attached to one another by "tip links," structures which link the tips of one cilium to another. Stretching and compressing, the tip links may open an ion channel and produce the receptor potential in the hair cell. Recently it has been shown that cdh23 and pchh15 are the adhesion molecules associated with these tip links. It is thought that a calcium driven motor causes a shortening of these links to regenerate tensions. This regeneration of tension allows for apprehension of prolonged auditory stimulation.

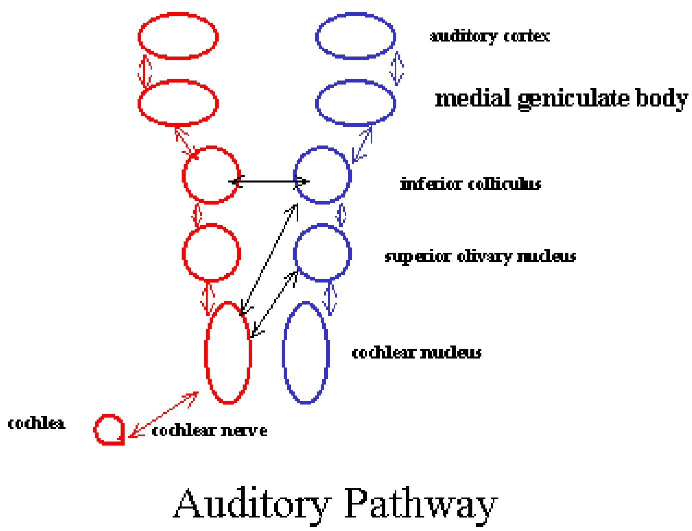
Neurons

Afferent neurons innervate cochlear inner hair cells, at synapses where the neurotransmitter glutamate communicates signals from the hair cells to the dendrites of the primary auditory neurons.

There are far fewer inner hair cells in the cochlea than afferent nerve fibers. The neural dendrites belong to neurons of the auditory nerve, which in turn joins the vestibular nerve to form the vestibulocochlear nerve, or cranial nerve number VIII.

Efferent projections from the brain to the cochlea also play a role in the perception of sound. Efferent synapses occur on outer hair cells and on afferent (towards the brain) dendrites under inner hair cells

Central auditory system



Auditory pathway

This sound information, now re-encoded, travels down the vestibulocochlear nerve, through intermediate stations such as the cochlear nuclei and superior olivary complex of the brainstem and the inferior colliculus of the midbrain, being further processed at each waypoint. The information eventually reaches the thalamus, and from there it is relayed to the cortex. In the human brain, the primary auditory cortex is located in the temporal lobe.

Associated anatomical structures include:

Cochlear nucleus

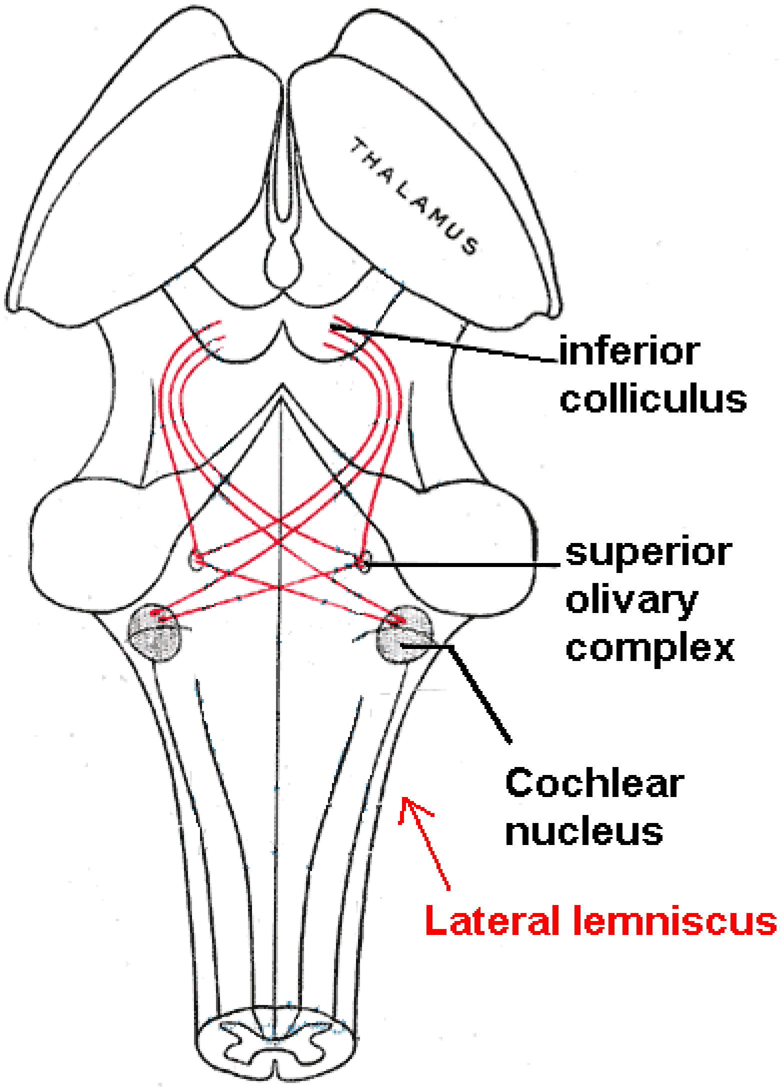
The cochlear nucleus is the first site of the neuronal processing of the newly converted “digital” data from the inner ear. This region is anatomically and physiologically split into two regions, the dorsal cochlear nucleus (DCN), and ventral cochlear nucleus (VCN).

Trapezoid body

The Trapezoid body is a bundle of decussating fibers in the ventral pons that carry information used for binaural computations in the brainstem.

Superior olivary complex

The superior olivary complex is located in the pons, and receives projections predominantly from the ventral cochlear nucleus, although the posterior cochlear nucleus projects there as well, via the ventral acoustic stria. Within the superior olivary complex lies the lateral superior olive (LSO) and the medial superior olive (MSO). The former is important in detecting interaural level differences while the latter is important in distinguishing interaural time difference.



Lateral lemniscus in red, as it connects the cochlear nucleus, superior olivary nucleus and the inferior colliculus. Seen from behind.

Lateral lemniscus

The lateral lemniscus is a tract of axons in the brainstem that carries information about sound from the cochlear nucleus to various brainstem nuclei and ultimately the contralateral inferior colliculus of the midbrain.

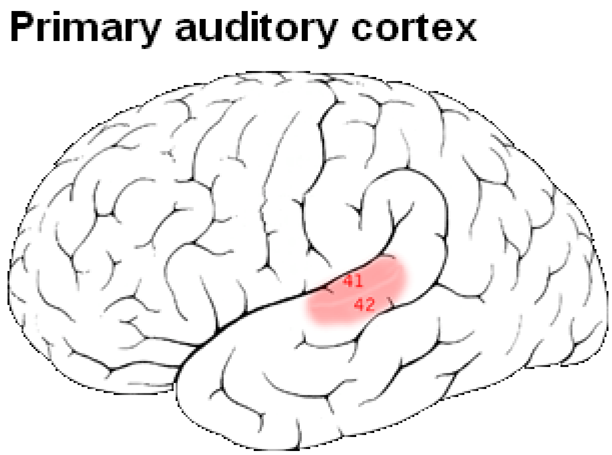
Inferior colliculi

The IC are located just below the visual processing centers known as the superior colliculi. The central nucleus of the IC is a nearly obligatory relay in the ascending auditory system, and most likely acts to integrate information (specifically regarding sound source localization from the superior olivary complex and dorsal cochlear nucleus) before sending it to the thalamus and cortex

Medial geniculate nucleus

The medial geniculate nucleus is part of the thalamic relay system.

Primary auditory cortex



The primary auditory cortex is the first region of cerebral cortex to receive auditory input.

Perception of sound is associated with the right posterior superior temporal gyrus (STG). The superior temporal gyrus contains several important structures of the brain, including Brodmann areas 41 and 42, marking the location of the primary auditory cortex, the cortical region responsible for the sensation of basic characteristics of sound such as pitch and rhythm.

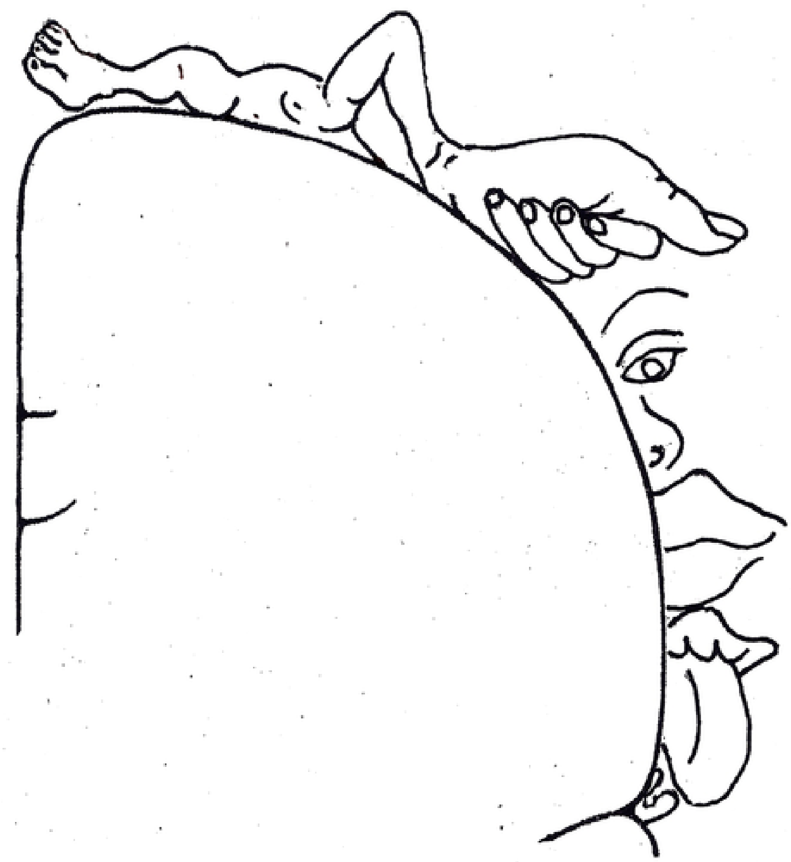
The auditory association area is located within the temporal lobe of the brain, in an area called the Wernicke's area, or area 22. This area, near the lateral cerebral sulcus, is an important region for the processing of acoustic signals so that they can be distinguished as speech, music, or noise.

Chapter 3

Somatosensory System

The **somatosensory system** is a diverse sensory system comprising the receptors and processing centres to produce the sensory modalities such as touch, temperature, proprioception (body position), and nociception (pain). The sensory receptors cover the skin and epithelia, skeletal muscles, bones and joints, internal organs, and the cardiovascular system. While **touch** (also, more formally, **tactition**; adjectival form: "tactile" or "somatosensory") is considered one of the five traditional senses, the impression of touch is formed from several modalities. In medicine, the colloquial term touch is usually replaced with **somatic senses** to better reflect the variety of mechanisms involved.

The system reacts to diverse stimuli using different receptors: thermoreceptors, nociceptors, mechanoreceptors and chemoreceptors. Transmission of information from the receptors passes via sensory nerves through tracts in the spinal cord and into the brain. Processing primarily occurs in the primary somatosensory area in the parietal lobe of the cerebral cortex.



The cortical homunculus was devised by Wilder Penfield

At its simplest, the system works when activity in a sensory neuron is triggered by a specific stimulus such as heat; this signal eventually passes to an area in the brain uniquely attributed to that area on the body—this allows the processed stimulus to be felt at the correct location. The point-to-point mapping of the body surfaces in the brain is called a homunculus and is essential in the creation of a body image. This brain-surface ("cortical") map is not immutable, however. Dramatic shifts can occur in response to stroke or injury.

Anatomy

The somatosensory system is spread through all major parts of a mammal's body (and other vertebrates). It consists both of sensory receptors and sensory (afferent) neurons in the periphery (skin, muscle and organs for example), to deeper neurones within the central nervous system.

General somatosensory pathway

A somatosensory pathway will typically have three long neurons: primary, secondary and tertiary (or first, second, and third).

- The **first** neuron always has its cell body in the dorsal root ganglion of the spinal nerve (if sensation is in head or neck, it will be the trigeminal nerve ganglia or the ganglia of other sensory cranial nerves).
- The **second** neuron has its cell body either in the spinal cord or in the brainstem. This neuron's ascending axons will cross (decussate) to the opposite side either in the spinal cord or in the brainstem. The axons of many of these neurones terminate in the thalamus (for example the ventral posterior nucleus, VPN), others terminate in the reticular system or the cerebellum.
- In the case of touch and certain types of pain, the **third** neuron has its cell body in the VPN of the thalamus and ends in the postcentral gyrus of the parietal lobe.

Periphery

In the periphery, the somatosensory system detects various stimuli by sensory receptors, e.g. by mechanoreceptors for tactile sensation and nociceptors for pain sensation. The sensory information (touch, pain, temperature etc.,) is then conveyed to the central nervous system by afferent neurones. There are a number of different types of afferent neurones which vary in their size, structure and properties. Generally there is a correlation between the type of sensory modality detected and the type of afferent neurone involved. For example, slow, thin, unmyelinated neurones conduct pain whereas faster, thicker, myelinated neurones conduct casual touch.

Spinal cord

In the spinal cord, the somatosensory system includes ascending pathways from the body to the brain. One major target within the brain is the postcentral gyrus in the cerebral cortex. This is the target for neurones of the Dorsal Column Medial Lemniscal pathway and the Ventral Spinothalamic pathway. Note that many ascending somatosensory pathways include synapses in either the thalamus or the reticular formation before they reach the cortex. Other ascending pathways, particularly those involved with control of posture are projected to the cerebellum. These include the ventral and dorsal spinocerebellar tracts. Another important target for afferent somatosensory neurones which enter the spinal cord are those neurones involved with local segmental reflexes.

Brain

The primary somatosensory area in the human cortex is located in the postcentral gyrus of the parietal lobe. The postcentral gyrus is the location of the *primary somatosensory area*, the main sensory receptive area for the sense of touch. Like other sensory areas, there is a map of sensory space called a homunculus at this location. For the primary somatosensory cortex, this is called the sensory homunculus. Areas of this part of the human brain map to certain areas of the body, dependent on the amount or importance of somatosensory input from that area. For example, there is a large area of cortex devoted to sensation in the hands, while the back has a much smaller area. Somatosensory information involved with proprioception and posture also targets an entirely different part of the brain, the cerebellum.

Physiology

Initiation of somatosensation begins with activation of a physical "receptor". These somatosensory receptors tend to lie in skin, organs or muscle. The structure of these receptors is broadly similar in all cases, consisting of either a "free nerve ending" or a nerve ending embedded in a specialised capsule. They can be activated by movement (mechanoreceptor), pressure (mechanoreceptor), chemical (chemoreceptor) and/or temperature. Another activation is by vibrations generated as a finger scans across a surface. This is the means by which we can sense fine textures in which the spatial scale is less than 200 μm. Such vibrations are around 250 Hz, which is the optimal frequency sensitivity of Pacinian corpuscles. In each case, the general principle of activation is similar; the stimulus causes depolarisation of the nerve ending and then an action potential is initiated. This action potential then (usually) travels inward towards the spinal cord.

Diseases

A somatosensory deficiency may be caused by a peripheral neuropathy involving peripheral nerves of the somatosensory system.

This may present as numbness or paresthesia.

Evaluation of any suspected disease of the somatosensory system is included in a neurological examination of the peripheral nervous system

Technology

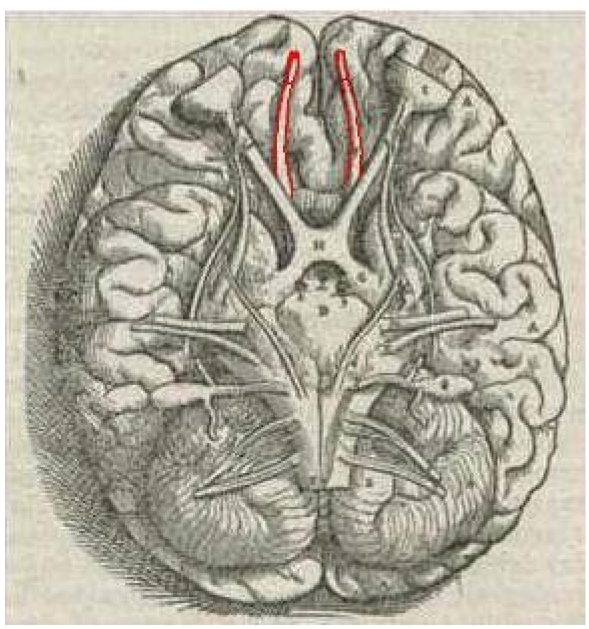
The new research area of haptic technology can provide touch sensation in virtual and real environments. This new discipline has started to provide critical insights into touch capabilities.

Chapter 4

Olfactory System

The **olfactory system** is the sensory system used for olfaction, or the sense of smell. Most mammals and reptiles have two distinct parts to their olfactory system: a **main olfactory system** and an accessory olfactory system. The main olfactory system detects volatile, airborne substances, while the accessory olfactory system senses fluid-phase stimuli. Behavioral evidence indicates that most often, the stimuli detected by the accessory olfactory system are awareness

The olfactory system is often spoken of along with the gustatory system as the **chemosensory senses** because both transduce chemical signals into perception.

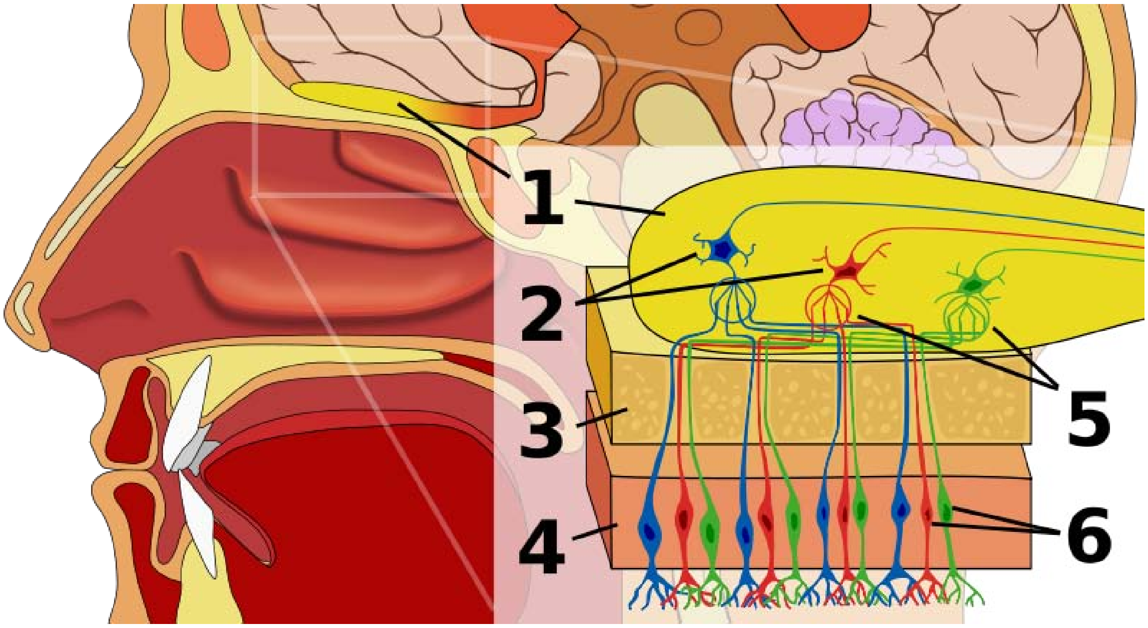


Vesalius' *Fabrica*, 1543. Human Olfactory bulbs and Olfactory tracts outlined in red

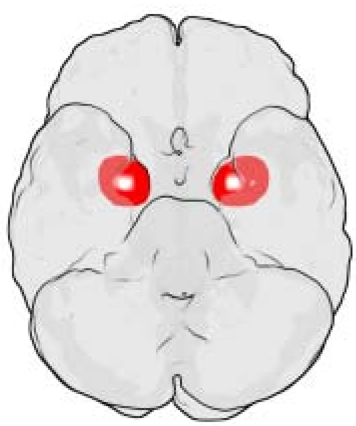
Function

The mechanism of the olfactory system can be divided into a peripheral one, sensing an external stimulus and encoding it as an electric signal in neurons, and a central one, where all signals are integrated and processed in the central nervous system.

Peripheral



1: Olfactory bulb 2: Mitral cells 3: Bone 4: Nasal Epithelium 5: Glomerulus 6: Olfactory receptor cells



Amygdala location in each hemisphere of the human brain

In mammals, the main olfactory system detects odorants that are inhaled through the nose, where they contact the main olfactory epithelium, which contains various olfactory receptors. These olfactory receptors are membrane proteins of bipolar olfactory receptor neurons in the olfactory epithelium. Rather than binding specific ligands like most receptors, olfactory receptors display affinity for a range of odor molecules. Olfactory neurons transduce receptor activation into electrical signals in neurons. The signals travel along the olfactory nerve, which belongs to the peripheral nervous system. This nerve terminates in the olfactory bulb, which belongs to the central nervous system. The complex set of olfactory receptors on different olfactory neurons can distinguish a new odor from the background environmental odors and determine the concentration of the odor.

Central

Axons from the olfactory sensory neurons converge in the olfactory bulb to form tangles called glomeruli (singular glomerulus). Inside the glomulerus, the axons contact the dendrites of mitral cells and several other types of cells. Mitral cells send their axons to a number of brain areas, including the anterior olfactory nucleus, piriform cortex, the medial amygdala, and the entorhinal cortex.

The piriform cortex is probably the area most closely associated with identifying the odor. The medial amygdala is involved in social functions such as mating and the recognition of animals of the same species. The entorhinal cortex is associated with memory, e.g. to pair odors with proper memories. The exact functions of these higher areas are a matter of scientific research and debate.

In the central nervous system, odors are represented as patterns of neural activity. These representations may be encoded by space (a pattern of activated neurons across a given olfactory region corresponds to the odor), time (a pattern of action potentials by multiple neurons corresponds to the odor) or a combination of the two. Scientists debate whether the odor code is primarily temporal or spatial.

Clinical implications

Damage to the olfactory system can occur by traumatic brain injury, cancer, infection, inhalation of toxic fumes, or neurodegenerative diseases such as Parkinson's disease and Alzheimer's disease. These conditions can cause anosmia. Doctors can detect damage to the olfactory system by presenting the patient with odors via a scratch and sniff card or by having the patient close their eyes and try to identify commonly available odors like coffee or peppermint candy.

Order of transmission to the brain

Name	Function
Olfactory receptor neuron	Is a cell with protruding cilia inside the Olfactory epithelium. The cilia or dendrites protrude into a layer of mucus where odorants are dissolved and detected. It is a bipolar neuron whose axions extend through the cribiform plate and synapse with the mitral cells located in the bulb of the olfactory nerve CN1. These are some of the only neurons capible of regeneration via basal cells.
Olfactory epithelium	Is specialized epithelium tissue that consists of olfactory cells, basal cells and supporting cells. The olfactory cells combine to form the olfactory nerve

Olfactory nerve	Leads directly away from the olfactory epithelium to the olfactory bulb.	
Olfactory bulb	Has two distinct and separate structures: the main olfactory bulb and the accessory olfactory bulb. It is made up of the following three layers of cells.	
	Glomerulus	Glomeruli are spherical structures that are separated by periglomerular cells and make up the first/outer layer of the olfactory bulb. It is in these structures that dendrites of mitral cells make contact with the olfactory nerves.
	Mitral cells	Are the main neuron cells of the olfactory bulb. Dendrites of the mitral cells reside in the glomeruli while the axons of the mitral cells merge together to form the lateral olfactory tract.
	Granule_cell	Act as inhibitory interneurons in the olfactory bulb.
Olfactory_tract	Made from the axons of mitral cells and connects the olfactory bulb to several parts of the brain.	
The brain	Anterior olfactory nucleus	Is one part of the brain that process odour information. It is located just behind the olfactory bulb. It passes information to several other parts of the brain, including the contralateral olfactory bulb, the piriform cortex, ipsilateral bulb and ipsilateral cortex.
	Piriform cortex	Also deals with the perception of odour information.
	Amygdala	Plays a major role in processing memory and emotional reactions.
	Entorhinal cortex	Receives information from all sensory systems. Plays an important part in memory.

History

Linda B. Buck and Richard Axel won the 2004 Nobel Prize in Physiology or Medicine for their work on the olfactory system.

Chapter 5

Mechanoreceptor

A **mechanoreceptor** is a sensory receptor that responds to mechanical pressure or distortion. There are four main types in the glabrous skin of humans: Pacinian corpuscles, Meissner's corpuscles, Merkel's discs, and Ruffini corpuscles. There are also mechanoreceptors in the hairy skin, and the hair cells in the cochlea are the most sensitive mechanoreceptors, transducing air pressure waves into sound.

Mechanism of sensation

Mechanoreceptors are primary neurons that respond to mechanical stimuli by firing action potentials. Peripheral transduction is believed to occur in the end-organs.

In somatosensory transduction, the afferent neurons transmit the message through synapses in the dorsal column nuclei, where the second order neurons send the signal to the thalamus and synapse with the third order neurons in the ventrobasal complex. The third order neurons then send the signal to the somatosensory cortex.

Feedback

More recent work has expanded the role of the cutaneous mechanoreceptors for feedback in fine motor control . Single action potentials from RAI and PC afferents are directly linked to activation of related hand muscles, whereas SAI activation does not trigger muscle activity.

History

The human work stemmed from Vallbo and Johansson's percutaneous recordings from human volunteers in the late 1970s, . Work in rhesus monkeys has found virtually identical mechanoreceptors with the exception of Ruffini corpuscles which are not found in the monkey.

Types

Cutaneous

Cutaneous mechanoreceptors are located in the skin, like other cutaneous receptors. They are all innervated by Aβ fibers, except the mechanorecepting free nerve endings, which are innervated by Aδ fibers. They can be categorized both by morphology, by what kind of sensation they perceive and by the rate of adaptation. Furthermore, they have different receptive field.

By morphology

- Ruffini's end organ detects tension deep in the skin.
- Meissner's corpuscle detects changes in texture (vibrations around 50 Hz); adapts rapidly.
- Pacinian corpuscle detects rapid vibrations (about 200-300 Hz).
- Merkel's disc detects sustained touch and pressure.
- Mechanorecepting Free nerve endings (touch, pressure, stretch)
- *Hair follicle receptors* are located in hair follicles and sense position changes of hairs.

By sensation

Cutaneous mechanoreceptors provide the senses of touch, pressure, vibration, proprioception and others.

- The **Slowly Adapting type 1 (SA1) mechanoreceptor**, with the Merkel cell end-organ, underlies the perception of form and roughness on the skin. They have small receptive fields and produce sustained responses to static stimulation.

- The **Slowly Adapting type 2 (SA2) mechanoreceptors** respond to skin stretch, but have not been closely linked to either proprioceptive or mechanoreceptive roles in perception. They also produce sustained responses to static stimulation, but have large receptive fields.

- The **Rapidly Adapting (RA) mechanoreceptor** underlies the perception of flutter and slip on the skin. They have small receptive fields and produce transient responses to the onset and offset of stimulation.

- **Pacinian receptors** underlie the perception of high frequency vibration. They also produce transient responses, but have large receptive fields.

By rate of adaptation

Cutaneous mechanoreceptors can also be separated into categories based on their rates of adaptation. When a mechanoreceptor receives a stimulus it begins to fire impulses or action potentials at an elevated frequency (the stronger the stimulus the higher the frequency). The cell, however, will soon “adapt” to a constant or static stimulus and the pulses will subside to a normal rate. Receptors that adapt quickly (i.e. quickly return to a normal pulse rate) are referred to as ‘’phasic’’. Those receptors that are slow to return to their normal firing rate are called ‘’tonic’’. Phasic mechanoreceptors are useful in sensing such things as texture, vibrations, etc; whereas tonic receptors are useful for temperature and proprioception among others.

- **Slowly adapting**

Slowly adapting mechanoreceptors include Merkel and Ruffini corpuscle end-organs, some free nerve endings.

-
    - Slowly adapting type I mechanoreceptors have multiple Merkel corpuscle end-organs.
    - Slowly adapting type II mechanoreceptors have single Ruffini corpuscle end-organs.

- **Intermediate adapting**

Some free nerve endings are intermediate adapting.

- **Rapidly adapting**

Rapidly adapting mechanoreceptors include Meissner corpuscle end-organs, Pacinian corpuscle end-organs, hair follicle receptors and some free nerve endings.

-
    - Rapidly adapting type I mechanoreceptors have multiple Meissner corpuscle end-organs.
    - Rapidly adapting type II mechanoreceptors (usually called Pacinian) have single Pacinian corpuscle end-organs.

Receptive field

Cutaneous mechanoreceptors with small, accurate receptive fields are found in areas needing accurate taction (e.g. the fingertips). In the fingertips and lips, innervation density of slowly adapting type I and rapidly adapting type I mechanoreceptors are greatly increased. These two types of mechanoreceptors have small discrete receptive fields and are thought to underlie most low threshold use of the fingers in assessing texture, surface slip, and flutter. Mechanoreceptors found in areas of the body with less tactile acuity tend to have larger receptive fields.

Others

Other mechanoreceptors than cutaneous ones include the hair cells, which are sensory receptors in the vestibular system in the inner ear, where they contribute to the auditory system and equilibrioception.

There are also Juxtacapillary (J) receptors, which respond to events such as pulmonary edema, pulmonary emboli, pneumonia, and barotrauma.

The Pacinian Corpuscle

Pacinian corpuscles are pressure receptors. They are located in the skin and also in various internal organs. Each is connected to a sensory neuron. Because of its relatively large size, a single Pacinian corpuscle can be isolated and its properties studied. Mechanical pressure of varying strength and frequency is applied to the corpuscle by the stylus. The electrical activity is detected by electrodes attached to the preparation.

Deforming the corpuscle creates a generator potential in the sensory neuron arising within it. This is a graded response: the greater the deformation, the greater the generator potential. If the generator potential reaches threshold, a volley of action potentials (also called nerve impulses) are triggered at the first node of Ranvier of the sensory neuron.

Once threshold is reached, the magnitude of the stimulus is encoded in the frequency of impulses generated in the neuron. So the more massive or rapid the deformation of a single corpuscle, the higher the frequency of nerve impulses generated in its neuron.

The optimal sensitivity of Pacinian Corpuscle is 250 Hz and this is the frequency range generated upon finger tips by textures made of features smaller than 200 µms.

Muscle Spindles and the Stretch Reflex

The knee jerk is a stretch reflex. Your physician taps you just below the knee with a rubber-headed hammer. You respond with an involuntary kick of the lower leg. The hammer strikes a tendon that inserts an extensor muscle in the front of the thigh into the lower leg. Tapping the tendon stretches the thigh muscle. This activates stretch receptors within the muscle called muscle spindles. Each muscle spindle consists of sensory nerve endings wrapped around special muscle fibers called spindle fibers (also called intrafusal fibers) Stretching a spindle fiber initiates a volley of impulses in the sensory neuron (a I-a neuron) attached to it. The impulses travel along the sensory axon to the spinal cord where they form several kinds of synapses:

Some of the branches of the I-a axons synapse directly with alpha motor neurons

(1). These carry impulses back to the same muscle causing it to contract. The leg straightens. Some of the branches of the I-a axons synapse with inhibitory interneurons in the spinal cord

(2). These, in turn, synapse with motor neurons leading back to the antagonistic muscle, a flexor in the back of the thigh. By inhibiting the flexor, these interneurons aid contraction of the extensor.

(3). Still other branches of the I-a axons synapse with interneurons leading to brain centers, e.g., the cerebellum, that coordinate body movements.

Chapter 6

Nociceptor

A **nociceptor** is a sensory receptor that responds to potentially damaging stimuli by sending nerve signals to the spinal cord and brain. This process, called nociception, usually causes the perception of pain.

History

Nociceptors were discovered by Charles Scott Sherrington in 1906. In earlier centuries, scientists believed that animals were like mechanical devices that transformed the energy of sensory stimuli into motor responses. Sherrington used many different styles of experiments to demonstrate that different types of stimulation to a nerve's receptive field led to different responses. Some intense stimuli trigger reflex withdrawal, autonomic responses and pain. The specific receptors for these intense stimuli were called nociceptors.

Location

In mammals, nociceptors are sensory neurons that are found in any area of the body that can sense pain either externally or internally. External examples are in tissues such as skin (cutaneous nociceptors), cornea and mucosa. Internal nociceptors are in a variety of organs, such as the muscle, joint, bladder, gut and continuing along the digestive tract. The cell bodies of these neurons are located in either the dorsal root ganglia or the trigeminal ganglia. The trigeminal ganglia are specialized nerves for the face, whereas the dorsal root ganglia associate with the rest of the body. The axons extend into the peripheral nervous system and terminate in branches to form receptive fields.

Development

Nociceptors develop from neural crest stem cells. The neural crest is responsible for a large part of early development in vertebrates. More specifically it is responsible for development of the peripheral nervous system. The neural crest stem cells split off from the neural tube as it closes, and nociceptors grow from the dorsal part of this neural crest tissue. They form late during neurogenesis. Earlier forming cells from this region can become non-pain sensing receptors; either proprioceptors or low-threshold mechanoreceptors. All neurons derived from neural crest, including embryonic nociceptors, express the TrkA nerve growth factor (NGF). However, transcription factors that determine the type of nociceptor remain unclear.

Following sensory neurogenesis, differentiation occurs and two different types of nociceptors are formed. They are classified as either peptidergic or nonpeptidergic nociceptors. The sets of receptors express distinct repertoires of ion channels and receptors. With their specialization, it allows the receptors to innervate different peripheral and central targets. This differentiation occurs in both perinatal and postnatal periods. The nonpeptidergic nociceptors switch off the TrkA nerve growth factor and begin expressing Ret. Ret is a transmembrane signaling component which allows for the expression of another growth factor—glial cell-derived growth factor (GDNF). This transition is assisted by Runx1 which has proven to be vital in the development of nonpeptidergic nociceptors. On the contrary, the peptidergic nociceptors continue to use TrkA and they express a completely different type of growth factor. Currently there is a lot of research being done to determine more specifically what creates the differences between nociceptors.

Types and functions

The peripheral terminal of the mature nociceptor is where the noxious stimuli are detected and transduced into electrical energy. When the electrical energy reaches a threshold value, an action potential is induced and driven towards the central nervous system (CNS). This leads to the train of events that allows for the conscious awareness of pain. The sensory specificity of nociceptors is established by the high threshold only to particular features of stimuli. Only when the high threshold has been reached by either chemical, thermal, or mechanical environments are the nociceptors triggered. The majority of nociceptors are classified by which of the environmental modalities they respond to. Some nociceptors respond to more than one of these modalities and are consequently designated polymodal. Other nociceptors respond to none of these modalities (although they may respond to stimulation under conditions of inflammation) and are referred to as sleeping or silent nociceptors.

Nociceptors have two different types of axons. The first are the Aδ fiber axons. They are myelinated and can allow an action potential to travel at a rate of about 20 meters/second towards the CNS. The other type is the more slowly conducting C fiber axons. These only conduct at speeds of around 2 meters/second. This is due to the light or non-myelination of the axon. As a result, pain comes in two phases. The first phase is mediated by the fast-conducting Aδ fibers and the second part due to (Polymodal) C fibers. The pain associated with the Aδ fibers can be associated to an initial extremely sharp pain. The second phase is a more prolonged and slightly less intense feeling of pain as a result from the damage. If there is massive or prolonged input to a C fiber there is progressive build up in the spinal cord dorsal horn. This phenomenon is similar to tetanus in muscles but is called wind-up. If wind-up occurs there is a probability of increased sensitivity to pain.

Thermal

Thermal nociceptors are activated by noxious heat or cold at various temperatures. There are specific nociceptor transducers that are responsible for how and if the specific nerve ending responds to the thermal stimulus. The first to be discovered was TRPV1, and it has a threshold that coincides with the heat pain temperature of 42°C. Other temperature in the warm-hot range is mediated by more than one TRP channel. Each of these channels express a particular C-terminal domain that corresponds to the warm-hot sensitivity. The interactions between all these channels and how the temperature level is determined to be above the pain threshold are unknown at this time. The cool stimuli are sensed by TRPM8 channels. Its C-terminal domain differs from the heat sensitive TRPs. Although this channel corresponds to cool stimuli, it is still unknown whether it also contributes in the detection of intense cold. An interesting finding related to cold stimuli is that tactile sensibility and motor function deteriorate while pain perception persists.

Mechanical

Mechanical nociceptors respond to excess pressure or mechanical deformation. They also respond to incisions that break the skin surface. The reaction to the stimulus is processed as pain by the cortex, just like chemical and thermal responses. These mechanical nociceptors frequently have polymodal characteristics. So it is possible that some of the transducers for thermal stimuli are the same for mechanical stimuli. The same is true for chemical stimuli, since TRPA1 appears to detect both mechanical and chemical changes.

Chemical

Chemical nociceptors have TRP channels that respond to a wide variety of spices commonly used in cooking. The one that sees the most response and is very widely tested is Capsaicin. Other chemical stimulants are environmental irritants like acrolein, a World War I chemical weapon and a component of cigarette smoke. Besides from these external stimulants, chemical nociceptors have the capacity to detect endogenous ligands, and certain fatty acid amines that arise from changes in internal tissues. Like in thermal nociceptors, TRPV1 can detect chemicals like capsaicin and spider toxins.

Sleeping/silent

Although each nociceptor can have a variety of possible threshold levels, some do not respond at all to chemical, thermal or mechanical stimuli unless injury actually has occurred. These are typically referred to as silent or sleeping nociceptors since their response comes only on the onset of inflammation to the surrounding tissue.

Pathway

Afferent nociceptive fibers (those that send information *to*, rather than *from* the brain) travel back to the spinal cord where they form synapses in its dorsal horn. This nociceptive fiber (located in the periphery) is a first order neuron. The cells in the dorsal horn are divided into physiologically distinct layers called laminae. Different fiber types form synapses in different layers, and use either glutamate or substance P as the neurotransmitter. Aδ fibers form synapses in laminae I and V, C fibers connect with neurons in lamina II, Aβ fibers connect with lamina I, III, & V. After reaching the specific lamina within the spinal cord, the first order nociceptive project to second order neurons and cross the midline. The second order neurons then send their information via two pathways to the thalamus: the dorsal column medial-lemniscal system and the anterolateral system. The first is reserved more for regular non-painful sensation, while the lateral is reserved for pain sensation. Upon reaching the thalamus, the information is processed in the ventral posterior nucleus and sent to the cerebral cortex in the brain. As there is an ascending pathway to the brain that initiates the conscious realization of pain, there also is a descending pathway which modulates pain sensory. The brain can request the release of specific hormones or chemicals that can have analgesic effects which can reduce or inhibit pain sensation. The area of the brain that stimulates the release of these hormones is the hypothalamus.

This effect of descending inhibition can be shown by electrically stimulating the periaqueductal grey area of the midbrain. The periaqueductal grey in turn projects to other areas involved in pain regulation, such as the nucleus raphe magnus (which also receives similar afferents from the nucleus reticularis paragigantocellularis (NPG). In turn the nucleus raphe magnus projects to the substantia gelatinosa region of the dorsal horn and mediates the sensation of spinothalamic inputs. The periaqueductal grey also contains opioid receptors which explains one of the mechanisms by which opioids such as morphine and diacetylmorphine exhibit an analgesic effect.

Sensitivity

Nociceptor neuron sensitivity is modulated by a large variety of mediators in the extracellular space. Peripheral sensitization represents a form of functional plasticity of the nociceptor. The nociceptor can change from being simply a noxious stimulus detector to a detector of non-noxious stimuli. The result is that low intensity stimuli from regular activity, initiates a painful sensation. This is commonly known as hyperalgesia. Inflammation is one common cause that results in the sensitization of nociceptors. Normally hyperalgesia ceases when inflammation goes down, however, sometimes genetic defects and/or repeated injury can result in allodynia: a completely non-noxious stimulus like light touch causes extreme pain. Allodynia can also be caused when a nociceptor is damaged in the peripheral nerves. This can result in deafferentation, which means the development of different central processes from the surviving afferent nerve. With this situation, surviving dorsal root axons of the nociceptors can make contact with the spinal cord, thus changing the normal input.

Nociceptors in non-mammalian animals

Nociception has been documented in non-mammalian animals, including fish and a wide range of invertebrates, including leeches, nematode worms, sea slugs, and fruit flies. Although these neurons may have different pathways and relationships to the central nervous system than mammalian nociceptors, nociceptive neurons in non-mammals often fire in response to similar stimuli as mammals, such as high temperature (40 degrees C or more), low pH, capsaicin, and tissue damage.

Terminology

Due to historical understandings of pain, nociceptors are also called pain receptors. This usage is not consistent with the modern definition of pain as a subjective experience.

Chapter 7

Chemoreceptor and Thermoreceptor

Chemoreceptor

A **chemoreceptor**, also known as **chemosensor**, is a sensory receptor that transduces a chemical signal into an action potential. In more general terms, a chemosensor detects certain chemical stimuli in the environment.

Classes

There are two main classes of the chemosensor: direct and distance.

- Examples of *distance chemoreceptors* are:
    - olfactory receptor neurons in the olfactory system
    - neurons in the vomeronasal organ that detect pheromones
- Examples of *direct chemoreceptors* include
    - Taste buds in the gustatory system
    - Carotid bodies and aortic bodies detect changes primarily in oxygen. They also sense increases in CO_2 partial pressure and decreases in arterial pH, but to a lesser degree than for O_2.
- The chemoreceptor trigger zone is an area of the medulla in the brain that receives inputs from blood-borne drugs or hormones, and communicates with the vomiting center.

Cellular antennae

Within the biological and medical disciplines, recent discoveries have noted that *primary cilia* in many types of cells within eukaryotes serve as *cellular antennae*. These cilia play important roles in chemosensation. The current scientific understanding of primary cilia organelles views them as "sensory cellular antennae that coordinate a large number of cellular signaling pathways, sometimes coupling the signaling to ciliary motility or alternatively to cell division and differentiation."

Systems affected

Breathing rate

Chemoreceptors detect the levels of carbon dioxide in the blood. To do this, they monitor the concentration of hydrogen ions in the blood, which decrease the pH of the blood. This is a direct consequence of an increase in carbon dioxide concentration, because carbon dioxide becomes carbonic acid in an aqueous environment.

The response is that the respiratory centre (in the medulla), sends nervous impulses to the external intercostal muscles and the diaphragm, via the intercostal nerve and the phrenic nerve, respectively, to increase breathing rate and the volume of the lungs during inhalation.

Chemoreceptors that affect breathing rate are broken down into two categories.

- central chemoreceptors are located on the ventrolateral surface of medulla oblongata and detect changes in pH of cerebrospinal fluid. They do not respond to a drop in oxygen, and eventually desensitize.

- peripheral chemoreceptors: Aortic body detects changes in blood oxygen and carbon dioxide, but not pH, while carotid body detects all three. They do not desensitize. Their effect on breathing rate is less than that of the central chemoreceptors.

Heart rate

Chemoreceptors in the medulla oblongata, carotid arteries, and aortic arch detect the levels of carbon dioxide in the blood, in the same way as applicable in the Breathing Rate section.

In response to this high concentration, a nervous impulse is sent to the cardiovascular centre in the medulla, which will then feedback to the sympathetic ganglia, increasing nervous impulses here, and prompting the sinoatrial node to stimulate more contractions of the myogenic cardiac muscle, increasing heart rate by causing the secretion of nor-adrenaline directly on to the sinoatrial node.

Sense organs

In taste sensation, the tongue is composed of 5 different taste buds: salty, sour, sweet, bitter, and savory. The salty and sour tastes work directly through the ion channels, the sweet and bitter taste work through G protein-coupled receptors, and the savory sensation is activated by glutamate.

Noses in vertebrates and antennae in many invertebrates act as distance chemoreceptors. Molecules are diffused through the air and bind to specific receptors on *olfactory sensory neurons*, activating an opening ion channel via G-proteins.

When inputs from the environment are significant to the survival of the organism, the input must be detected. As all life processes are ultimately based on chemistry it is natural that detection and passing on of the external input will involve chemical events. The chemistry of the environment is, of course, relevant to survival, and detection of chemical input from the outside may well articulate directly with cell chemicals.

For example: The emissions of a predator's food source, such as odors or pheromones, may be in the air or on a surface where the food source has been. Cells in the head, usually the air passages or mouth, have chemical receptors on their surface that change when in contact with the emissions. The change does not stop there. It passes in either chemical or electrochemical form to the central processor, the brain or spinal cord. The resulting output from the CNS (central nervous system) makes body actions that will engage the food and enhance survival.

Thermoreceptor

A **thermoreceptor** is a sensory receptor, or more accurately the receptive portion of a sensory neuron, that codes absolute and relative changes in temperature, primarily within the innocuous range. In the mammalian peripheral nervous system warmth receptors are thought to be unmyelinated C-fibres (low conduction velocity), while those responding to cold have both C-fibers and thinly myelinated A delta fibers (faster conduction velocity). The adequate stimulus for a warm receptor is warming, which results in an increase in their action potential discharge rate. Cooling results in a decrease in warm receptor discharge rate. For cold receptors their firing rate increases during cooling and decreases during warming. Some cold receptors also respond with a brief action potential discharge to high temperatures, i.e. typically above 45°C, and this is known as a paradoxical response to heat. The mechanism responsible for this behavior has not been determined. A special form of thermoreceptor is found in some snakes, the viper pit organ and this specialized structure is sensitive to energy in the infrared part of the spectrum.

Location

In mammals, temperature receptors innervate various tissues including the skin (as cutaneous receptors), cornea and urinary bladder. Neurons from the pre-optic and hypothalamic regions of the brain that respond to small changes in temperature have also been described, providing information on core temperature. The hypothalamus is involved in thermoregulation, the thermoreceptors allowing feed-forward responses to a predicted change in core body temperature in response to changing environmental conditions.

Structure

Thermoreceptors have been classically described as having 'free' non-specialised endings; the mechanism of activation in response to temperature changes is not completely understood.

Function

Cold-sensitive thermoreceptors give rise to the sensations of cooling, cold and freshness. In the cornea cold receptors are thought to respond with an increase in firing rate to cooling produced by evaporation of lacrimal fluid 'tears' and thereby to elicit a reflex blink.

Location

Warm and cold receptors play a part in sensing innocuous environmental temperature. Temperatures likely to damage an organism are sensed by sub-categories of nociceptors that may respond to noxious cold, noxious heat or more than one noxious stimulus modality (i.e., they are polymodal). The nerve endings of sensory neurons that respond preferentially to cooling are found in moderate density in the skin but also occur in relatively high spatial density in the cornea, tongue, bladder, and facial skin. The speculation is that lingual cold receptors deliver information that modulates the sense of taste; i.e. some foods taste good when cold, while others do not.

Mechanism of transduction

This area of research has recently received considerable attention with the identification and cloning of the Transient Receptor Potential (TRP) family of proteins. The transduction of temperature in cold receptors is mediated in part by the TRPM8 channel. This channel passes a mixed inward cationic (predominantly carried by Na^+ ions although the channel is also permeable to Ca^{2+}) current of a magnitude that is inversely proportional to temperature. The channel is sensitive over a temperature range spanning about 10-35°C. TRPM8 can also be activated by the binding of an extracellular ligand. Menthol can activate the TRPM8 channel in this way. Since the TRPM8 is expressed in neurons whose physiological role is to signal cooling, menthol applied to various bodily surfaces evokes a sensation of cooling. The feeling of freshness associated with the activation of cold receptors by menthol, particularly those in facial areas with axons in the trigeminal (V) nerve, accounts for its use in numerous toiletries including toothpaste, shaving lotions, facial creams and the like. Another molecular component of cold transduction is the temperature dependence of so-called leak channels which pass an outward current carried by potassium ions. Some leak channels derive from the family of two-pore (2P) domain potassium channels. Amongst the various members of the 2P-domain channels, some close quite promptly at temperatures less than about 28°C (eg.

TRAAK, TREK). Temperature also modulates the activity of the Na^+/K^+-ATPase. The Na^+/K^+-ATPase is a P-type pump that extrudes $3Na^+$ ions in exchange for $2K^+$ ions for each hydrolytic cleavage of ATP. This results in a net movement of positive charge out of the cell, i.e. a hyperpolarizing current. The magnitude of this current is proportional to the rate of pump activity. It has been suggested that it is the constellation of various thermally sensitive proteins together in a neuron that gives rise to a cold receptor. This emergent property of the neuron is thought to comprise, the expression of the aforementioned proteins as well as various voltage-sensitive channels including the hyperpolarization-activated, cyclic nucleotide-gated (HCN) channel and the rapidly activating and inactivating transient potassium channel (IK_A).

Chapter 8

Active Sensory Systems and Equilibrioception

Active sensory systems

Active sensory systems are sensory receptors that are activated by probing the environment with self-generated energy. Examples include echolocation of bats and dolphins and insect antennae. Using self-generated energy allows more control over signal intensity, direction, timing and spectral characteristics. By contrast, passive sensory systems involve activation by ambient energy. For example, human vision relies on using light from environment instead of generating own source.

Active sensory systems receive information with or without direct contact. **Teleceptive Active Sensory Systems** collect information by directing propagating energy and detecting objects using cues such as time delay and intensity of return signal. Examples include echolocation of bats and electrosensory detection of electric fish. **Contact Active Sensory Systems** use physical contact between stimuli and organism. Insect antennae and whiskers are examples of contact active sensory systems.

Examples of Active Sensory Systems

Active Electrolocation

1. **Bioluminescence** Adult firefly uses self-generated light to locate mates. In deep oceans, barbeled dragonfish produces near infrared light.
2. **Electrostatic field** Electric fishes probe the environment and create active hydrodynamic imaging.

Mechanosensory

1. **Active touching** Nocturnal animals depend on whiskers to navigate by gathering information about position, size, shape, orientation and texture of objects. Insects use antennae to probe the environment during locomotion. Human's reaching out to objects with hands is an analogy.

Echolocation

1. **Echolocation** Active acoustic sensing of self-produced sounds. Bats emit echolocation calls for detecting prey in flight. Dolphins and killer-whales use echolocation in water.

Chemical

1. Because propagation of chemicals take longer than other sources, only organisms with slow locomotion can utilize chemical signals to probe the environment. The slime mold *Dictyostelium discoideum* uses ammonia to probe the environment to avoid obstacles during formation of fruiting body. Deploying chemical signal is also limited by lack of return signals .

Physical and Ecological Constraints

Energy Propagation

An important constraint in teleceptive active sensory systems is generating energy with return signal above threshold of detection. Self-generated energy needs to be strong enough to detect objects at a distance. Due to geometric spreading, energy emitted uniformly will spread over a sphere of increasing surface area. Signal strength depends on the square of distance between organism and target. In teleceptive active sensing, geometric spread cost is doubled, because signal is emitted and returned. As a result, fraction of energy returned is only a fourth power of the distance between organism and target.

Directionality also plays a role in energy expenditure in producing signals. Increase in directionality and narrow range result in longer attenuation length. Bat has a wider detection range to target small insects flying at high velocity. Dolphin produces a more narrow echolocation beam which propagates further. Electric fishes emit signals that envelope the whole body, thus has shorter length.

Attenuation

In addition to geometric spreading, absorption and scattering of energy during propagation results in the loss of energy. The attenuation length is the distance at which intensity drops to 1/e(37%) to initial intensity. Environmental factors such as fog, rain and turbulence disturb signal transmission and decreases attenuation length.

Length of Appendages

For contact sensory system, only targets within reach of contact appendages are detectable. Increase in length of appendages adds physical energy costs by adding weight during locomotion and investment for growth. As a compromise, whiskers of rats cover only the 35% of body. To minimize cost, rhythmic movements are coupled with stepping mechanisms of insects.

Conspicuousness

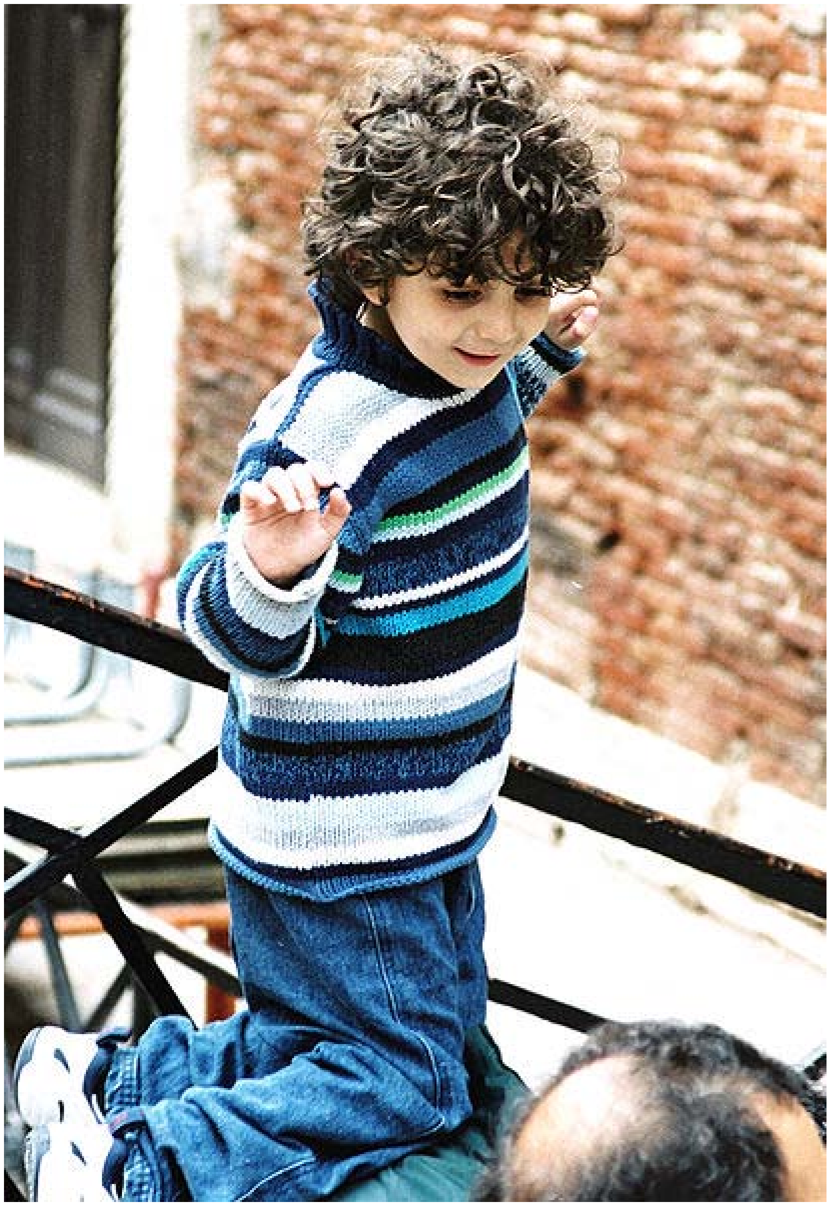
Energy released into the environment by organisms is prone to detection by other organisms. The detection by predators and competing individuals of same species provides a strong evolutionary pressure. When active sensing is used, energy detected at target is greater than returning signal. Prey or predators evolved to eavesdrop on active sensing signals. For example, most flying insect preys of bats developed sensitivity to echolocation call frequency. When stimulated by a high-pitched sound, moths engage in dodging flight pathway. Dolphins can also detect killer whales' ultrasonic clicks. In return, killer whales produce more irregular, isolated sonar clicks to make less conspicuous signals . In case of barbeled dragonfish, it utilizes red light that other deep-sea fishes can't detect.

Related Concepts

Corollary Discharge refers to the ability to differentiate one's own movements and responses to external motor events. Orientation and actions are mapped on neuronal level and remembered in the brain. Corollary discharge allows one to incorporate sensory intake as a result of sensory system and serves as a feedback system.
Jamming Avoidance Response Conspecific signals interfere active sensing of individuals sharing habitats. Electric fishes such as Eigenmannia developed reflexive shift in discharge frequencies in order to avoid frequency interference.

Equilibrioception

Equilibrioception or **sense of balance** is one of the physiological senses. It helps prevent humans and animals from falling over when walking or standing still.



Boy balancing on a man's backpack

Normal balance functioning

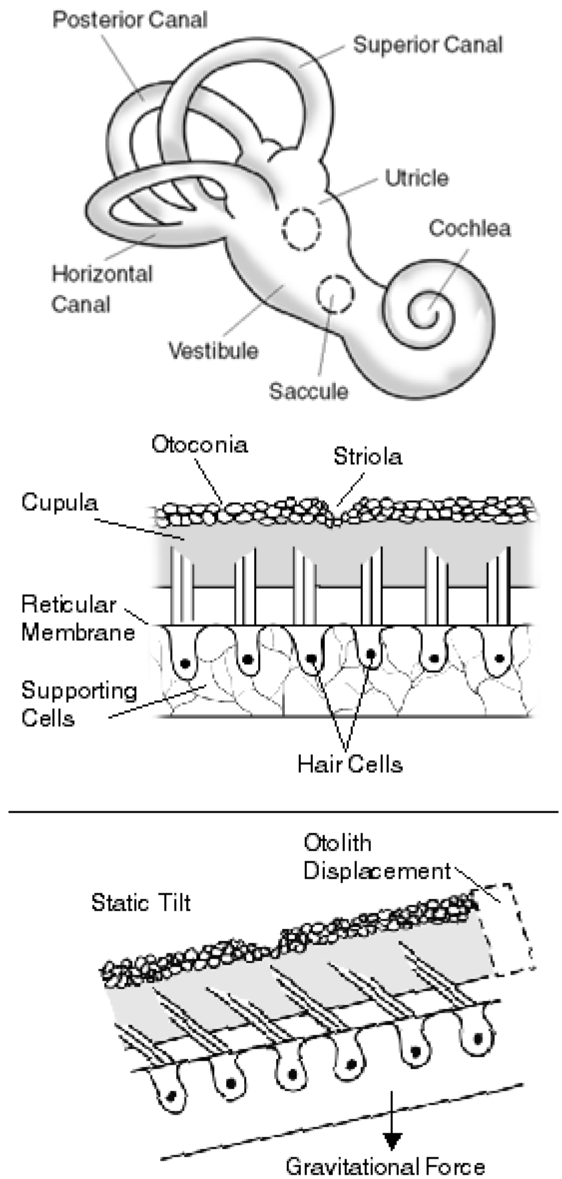
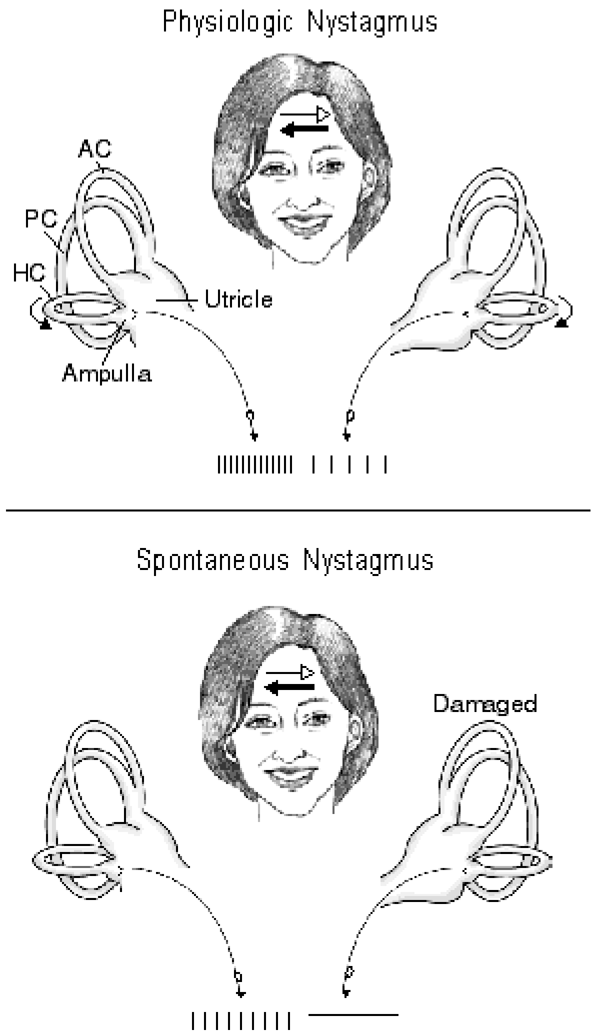


Illustration of the flow of fluid in the ear, which in turn causes displacement of the top portion of the hair cells that are embedded in the jelly-like cupula. Also shows the utricle and saccule organs that are responsible for detecting linear acceleration, or movement in a straight line.



This figure shows nerve activity associated with rotational-induced physiologic nystagmus and spontaneous nystagmus resulting from a lesion of one labyrinth. Thin straight arrows - direction of slow components; thick straight arrows - direction of fast components; curved arrows - direction of endolymph flow in the horizontal semicircular canals: AC - anterior canal, PC - posterior canal, HC - horizontal canal.

Balance is the result of a number of body systems working together. Specifically, in order to achieve balance the eyes (visual system), ears (vestibular system) and the body's sense of where it is in space (proprioception) ideally need to be intact.

The vestibule is the region of the inner ear where the semicircular canals converge,close to the cochlea (the hearing organ). The vestibular system works with the visual system to keep objects in focus when the head is moving. This is called the vestibulo-ocular reflex (VOR).

Movement of fluid in the semicircular canals signals the brain about the direction and speed of rotation of the head - for example, whether we are nodding our head up and down or looking from right to left. Each semicircular canal has a bulbed end, or enlarged portion, that contains hair cells. Rotation of the head causes a flow of fluid, which in turn causes displacement of the top portion of the hair cells that are embedded in the jelly-like cupula. Two other organs that are part of the vestibular system are the utricle and saccule. These are called the otolithic organs and are responsible for detecting linear acceleration, or movement in a straight line. The hair cells of the otolithic organs are blanketed with a jelly-like layer studded with tiny calcium stones called otoconia. When the head is tilted or the body position is changed with respect to gravity, the displacement of the stones causes the hair cells to bend.

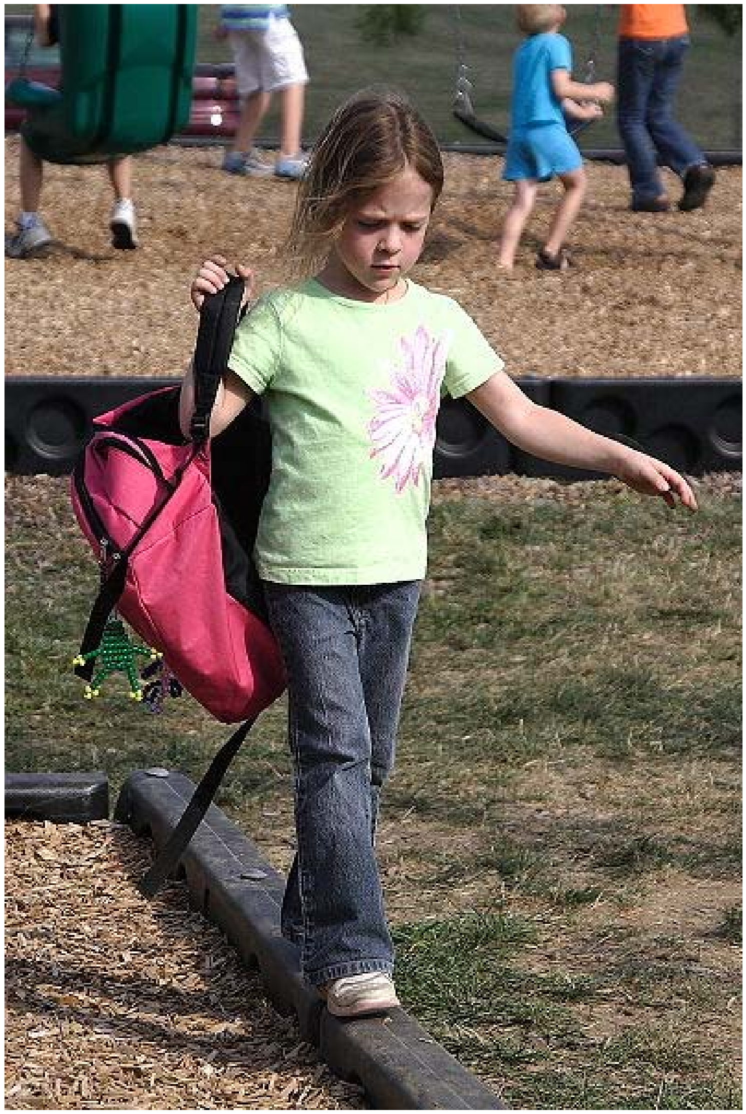
The balance system works with the visual and skeletal systems (the muscles and joints and their sensors) to maintain orientation or balance. For example, visual signals are sent to the brain about the body's position in relation to its surroundings. These signals are processed by the brain, and compared to information from the vestibular, visual and the skeletal systems.

In humans

In humans, equilibrioception is mainly sensed by the detection of acceleration, which occurs in the vestibular system. Other senses play roles as well, e.g. the visual system and proprioception. The importance of visual input for balance is illustrated by its being harder to stand on one foot with eyes closed than with eyes open.

The sense of balance, usually, deteriorates in the process of aging of a person. However, it can be improved considerably with the help of special training.

Vestibular system



Balance skill development in children

In the vestibular system, equilibrioception is determined by the level of fluid properly called endolymph in the labyrinth - a complex set of tubing in the inner ear.

Dysfunction

When the sense of balance is interrupted it causes dizziness, disorientation and nausea. Balance can be upset by Ménière's disease, superior canal dehiscence syndrome, an inner ear infection, by a bad common cold affecting the head or a number of other medical conditions. It can also be temporarily disturbed by quick or prolonged acceleration, for example riding on a merry-go-round. Blows can also affect equilibrioreception, especially those to the side of the head or directly to the ear.

Most astronauts find that their sense of balance is impaired when in orbit because they are in a constant state of weightlessness. This causes a form of motion sickness called space adaptation syndrome.

In animals

Some animals have better equilibrioception than humans, for example a cat uses its inner ear and tail to walk on a thin fence.

Equilibrioception in many marine animals is done with an entirely different organ, the statocyst, which detects the position of tiny calcareous stones to determine which way is "up".

In plants

Poplar stems can detect reorientation and inclination.

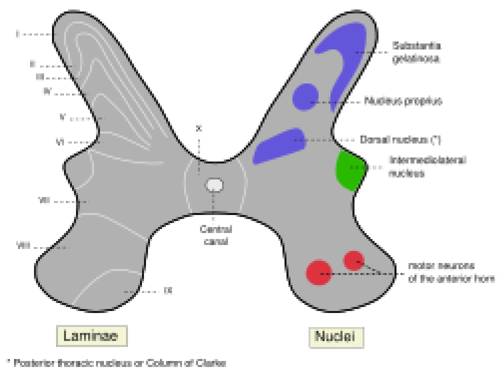
Training devices

- balance ball
- balance board
- balance bicycle
- BOSU
- slackline
- tight rope

Chapter 9

Group C Nerve Fiber

Group C nerve fiber



C fiber not labeled, but substantia gelatinosa of Rolando is Rexed lamina II, labeled at upper left.

Structure and Anatomy

Location

C fibers are found in the peripheral nerves of the somatic sensory system. They are afferent fibers, conveying input signals from the periphery to the central nervous system.

Structure

C fibres are unmyelinated unlike most other fibers in the nervous system. This lack of myelination is the cause of their slow conduction velocity, which is on the order of no more than 2 m/s. C fibers are on average 0.2-1.5 μm in diameter. The other main classification of nociceptors is Aδ fibers. These fibers have axons that are larger (1-5 μm), in diameter, are myelinated, and have a higher conduction velocity, which is on the order of about 20 m/s.

Remak bundles

C fiber axons are grouped together into what is known as Remak bundles. These occur when an unmyelinated Schwann cell bundles the axons close together by surrounding them. The Schwann cell keeps them from touching each other by squeezing its cytoplasm between the axons. The condition of Remak bundles varies with age. The number of C fiber axons in each Remak bundle varies with location. For example in a rat model, large bundles of greater than 20 axons are found exiting the L5 dorsal root ganglion, while smaller bundles of average 3 axons are found in distal nerve segments. Multiple neurons contribute axons to the Remak bundle with an average ratio of about 2 axons contributed per bundle. The cross sectional area of a Remak bundle is proportional to the number of axons found inside it. Remak bundles in the distal peripheral nerve are clustered with other Remak bundles. The Remak Schwann cells have been shown to be electrochemically responsive to action potentials of the axons contained within them.

In experiments where nerve injury is caused but nearby C fibers remain intact, increased spontaneous activity in the C fibers is observed. This phenomenon supports the theory that damaged nerve fibers may release factors that alter the function of neighboring undamaged fibers. Study of Remak bundles has important implications in nerve regeneration after sustaining injury. Currently, recovery of distal C fiber function takes months and may still only regain incomplete function. This may result in abnormal sensory function or neuropathic pain. Remak bundles are thought to release certain trophic factors that promote the regeneration of the damaged axons.

Pathway

C fibers synapse to second-order projection neurons in the spinal cord at the upper laminae of the dorsal horn in the substantia gelatinosa. The second-order projection neurons are of the wide dynamic range (WDR) type, which receive input from both nociceptive terminals as well as myelinated A-type fibers. There are three types of second order projection neurons in the spinothalamic tract: wide dynamic range (WDR), high threshold (HT), and low threshold (LT). These classifications are based on their responses to mechanical stimuli. The second-order neurons ascend to the brain stem and thalamus in the ventrolateral, or anterolateral, quadrant of the contralateral half of the spinal cord, forming the spinothalamic tract. The spinothalamic tract is the main pathway associated with pain and temperature perception, which immediately crosses the spinal cord laterally. This crossover feature is clinically important because it allows for identification of the location of injury.

Function

Because of their higher conduction velocity, Aδ fibers are responsible for the sensation of a sharp first pain. They respond to a weaker intensity of stimulus. C fibers, however, respond to a stronger intensity of stimulus and are responsible for the slow, dull, longer-lasting, second pain.

C fibers are considered polymodal because they can respond to thermal, mechanical, and chemical stimuli. C fibers respond to all kinds of physiological changes in the body. For example, they can respond to hypoxia, hypoglycemia, hypo-osmolarity, the presence of muscle metabolic products, and even light or sensitive touch. C fiber receptors include:

- C fiber nociceptors
  - responsible for the second, burning pain
- C fiber warming specific receptors
  - responsible for warmth
- ultra-slow histamine-selective C fibers
  - responsible for itch
- tactile C fibers
  - sensual touch
- C mechano- and metabo- receptors in muscles or joints
  - responsible for muscle exercise, burn and cramp

This variation of input signals calls for a variety of cells of the cortex in lamina 1 to have different modality-selectiveness and morphologies. These varying neurons are responsible for the different feelings we perceive in our body and can be classified by their responses to ranges of stimuli. The brain uses the integration of these signals to maintain homeostasis in the body whether it is temperature related or pain related.

Vanilloid Receptor

The vanilloid receptor (VR-1, TRPV1) is a receptor that is found on the free nerve endings of both C and Aδ fibers that responds to elevated levels of heat (>43°C) and the chemical capsaicin. Capsaicin activates C fibers by opening a ligand-gated ion channel and causing an action potential to occur. Because this receptor responds to both capsaicin and heat, chili peppers are sensed as hot. VR-1 is also able to respond to extracellular acidification and can integrate simultaneous exposure to all three sensory stimuli. VR1 is essential for the inflammatory sensitization to noxious thermal stimuli. A second type of receptor, a vanilloid-like receptor (TRPV2,VRL-1), has a higher threshold of activation regarding heat of about 52°C and also responds to capsaicin and low pH. Both types of receptors are transmembrane receptors that are closed during resting conditions. When open, these receptors allow for an influx of sodium and calcium which initiates an action potential across the fibers. Both receptors are part of a larger family of receptors called transient receptor potential (TRP) receptors. If damage to these heat transducer receptors occurs, the result can be chronic neuropathic pain caused by lowering the heat pain threshold for their phosphorylation.

Role in Neuropathic Pain

Activation of nociceptors is not necessary to cause the sensation of pain. Damage or injury to nerve fibers that normally respond to innocuous stimuli like light touch may lower their activation threshold needed to respond; this change causes the organism to feel intense pain from the lightest of touch. Neuropathic pain syndromes are caused by lesions or diseases of the parts of the nervous system that normally signal pain. There are four main classes:

- peripheral focal and multifocal nerve lesions
    - traumatic, ischemic or inflammatory
- peripheral generalized polyneuropathies
    - toxic, metabolic, hereditary or inflammatory
- CNS lesions
    - stroke, multiple sclerosis, spinal cord injury
- complex neuropathic disorders
    - complex regional pain syndromes [CRPSs]

After a nerve lesion of either C fibers or Aδ fibers, they become abnormally sensitive and cause pathological spontaneous activity. This alteration of normal activity is explained by molecular and cellular changes of the primary afferent nociceptors in response to the nerve damage. The abnormal activity of the damaged nerves is associated with the increased presence of mRNA for voltage-gated sodium channels. Irregular grouping of these channels in sites of the abnormal activity may be responsible for lowering the activation threshold, thus leading to hyperactivity.

Central Sensitization

After nerve damage or repeated stimulation, WDR (wide dynamic range) neurons experience a general increase in excitability. This hyper-excitability can be caused by an increased neuronal response to a noxious stimulus (hyperalgesia), a larger neuronal receptive field, or spread of the hyper-excitability to other segments. This condition is maintained by C fibers. C fibers cause central sensitization of the dorsal horn in the spinal cord in response to their hyperactivity. The mechanism underlying this phenomenon involves the release of glutamate by these pathologically sensitized C fibers. The glutamate interacts with the postsynaptic NMDA receptors, which aids the sensitization of the dorsal horn. Presynaptic neuronal voltage-gated N-calcium channels are largely responsible for the release of this glutamate as well as the neuropeptide, substance P. The expression of presynaptic neuronal voltage-gated N-calcium channels increases after a nerve lesion or repeated stimulation. NMDA receptor activation (by glutamate) enhances postsynaptic Nitric Oxide Synthase. Nitric Oxide is thought to migrate back to the presynaptic membrane to enhance the expression of the voltage-gated N-calcium channels resulting in a pain wind-up phenomenon. This abnormal central sensitization cycle results in increased pain (hyperalgesia) and pain responses from previously non-noxious stimuli evoke a pain response (allodynia).

Central sensitization of the dorsal horn neurons that is evoked from C fiber activity is responsible for temporal summation of “second pain” (TSSP). This event is called ‘windup’ and relies on a frequency greater or equal to 0.33Hz of the stimulus. Windup is associated with chronic pain and central sensitization. This minimum frequency was determined experimentally by comparing healthy patient fMRI’s when subjected to varying frequencies of heat pulses. The fMRI maps show common areas activated by the

TSSP responses which include contralateral thalamus (THAL), S1, bilateral S2, anterior and posterior insula (INS), mid-anterior cingulate cortex (ACC), and supplemental motor areas (SMA). TSSP events are also associated with other regions of the brain that process functions such as somatosensory processing, pain perception and modulation, cognition, pre-motor activity in the cortex.

Treatment

Currently, the availability of drugs proven to treat neuropathic pain is limited and varies widely from patient to patient. Many developed drugs have either been discovered by accident or by observation. Some past treatments include opiates like poppy extract, non-steroidal anti-inflammatory drugs like salicylic acid, and cocaine. Other recent treatments consist of antidepressants and anticonvulsants, although no substantial research on the actual mechanism of these treatments has been performed. However, patients respond differently to these treatments possibly because of gender differences or genetic backgrounds. Therefore, researchers have come to realize that no one drug or one class of drugs will reduce all pain. Research is now focusing on the underlying mechanisms involved in pain perception and how it can go wrong in order to develop an appropriate drug for patients afflicted with neuropathic pain.

Microneurography

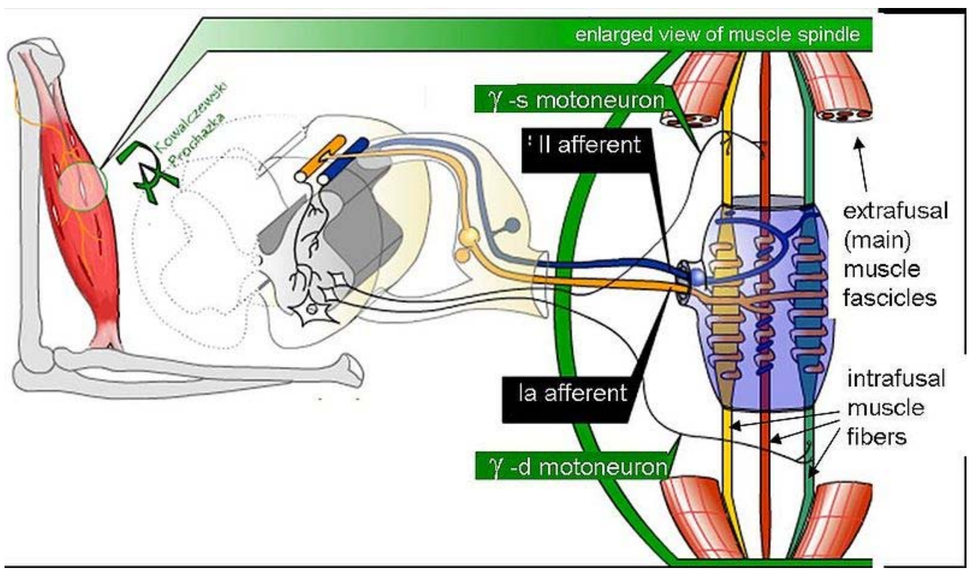
Microneurography is a technique using metal electrodes to observe neural traffic of both myelinated and unmyelinated axons in efferent and afferent neurons of the skin and muscle. This technique is particularly important in research involving C fibers. Single action potentials from unmyelinated axons can be observed. Recordings from efferent postganglionic sympathetic C fibers of the muscles and skin yield important insights into the neural control autonomic effector organs like blood vessels and sweat glands. Readings of afferent discharges from C nociceptors identified by marking method have also proved as important tools to revealing the mechanisms underlying sensations such as itch.

Unfortunately, interpretation of the microneurographic readings can be difficult because axonal membrane potential can not be determined from this method. A supplemental method used to better understand these readings involves examining recordings of post-spike excitability and shifts in latency; these features are associated with changes in membrane potential of unmyelinated axons like C fibers. Moalem-Taylor et al. experimentally used chemical modulators with known effects on membrane potential to study the post-spike super-excitability of C fibers. The researchers found three resulting events. Chemical medulators can produce a combination of loss of super-excitability along with increased axonal excitability, indicating membrane depolarization. Secondly, membrane hyperpolarization can result from a blockade of axonal hyperpolarization-activated current. Lastly, a non-specific increase in surface charge and a change in the voltage-dependent activation of sodium channels results from the application of calcium.

Chapter 10

Muscle Spindle and Neural Adaptation

Muscle spindle



Mammalian muscle spindle showing typical position in a muscle (left), neuronal connections in spinal cord (middle) and expanded schematic (right). The spindle is a stretch receptor with its own motor supply consisting of several intrafusal muscle fibres. The sensory endings of a primary (group Ia) afferent and a secondary (group II) afferent coil around the non-contractile central portions of the intrafusal fibres. Gamma motoneurons activate the intrafusal muscle fibres, changing the resting firing rate and stretch-sensitivity of the afferents.

Muscle spindles are sensory receptors within the belly of a muscle, which primarily detect changes in the length of this muscle. They convey length information to the central nervous system via sensory neurons. This information can be processed by the brain to determine the position of body parts. The responses of muscle spindles to changes in length also play an important role in regulating the contraction of muscles, by activating motoneurons via the stretch reflex to resist muscle stretch.

Anatomy

Muscle spindles are found within the belly of muscles, embedded in extrafusal muscle fibers. Note that "fusus" is the Latin word for spindle. Muscle spindles are composed of 3-12 intrafusal muscle fibers, of which there are three types:

- dynamic nuclear bag fibers (bag_1 fibers)
- static nuclear bag fibers (bag_2 fibers)
- nuclear chain fibers and the axons of sensory neurons.

Axons of gamma motoneurons also terminate in muscle spindles; they make synapses at either or both of the ends of the intrafusal muscle fibers and regulate the sensitivity of the sensory afferents, which are located in the non-contractile central (equatorial) region.

Muscle spindles are encapsulated by connective tissue, and are aligned parallel to extrafusal muscle fibers, unlike Golgi tendon organs, which are oriented in series.

The muscle spindle has both sensory and motor components.

- Primary and secondary sensory nerve fibers spiral around and terminate on the central portions of the intrafusal muscle fibers, providing the sensory component of the structure via stretch-sensitive ion-channels of the axons.
- In mammals including humans, the motor component is provided by up to a dozen gamma motoneurons and to a lesser extent by one or two beta motoneurons. Gamma and beta motoneurons are called fusimotor neurons, because they activate the intrafusal muscle fibers. Gamma motoneurons only innervate intrafusal muscle fibers, whereas beta motoneurons innervate both extrafusal and intrafusal muscle fibers and so are referred to as skeletofusimotor neurons.
- Fusimotor drive causes a contraction and stiffening of the end portions of the intrafusal muscle fibers.

Fusimotor neurons are classified as static or dynamic according to the type of intrafusal muscle fibers they innervate and their physiological effects on the responses of the Ia and II sensory neurons innervating the central, non-contractile part of the muscle spindle.

- The static axons innervate the chain or bag_2 fibers. They increase the firing rate of Ia and II afferents at a given muscle length.
- The dynamic axons innervate the bag_1 intrafusal muscle fibers. They increase the stretch-sensitivity of the Ia afferents by stiffening the bag_1 intrafusal fibers.

Sensitivity modification

The function of the gamma motoneurons is not to supplement the force of muscle contraction provided by the extrafusal fibers, but to modify the sensitivity of the muscle spindle sensory afferents to stretch. Upon release of acetylcholine by the active gamma motoneuron, the end portions of the intrafusal muscle fibers contract, thus elongating the non-contractile central portions. This opens stretch-sensitive ion channels of the sensory endings, leading to an influx of sodium ions. This raises the resting potential of the endings, thereby increasing the probability of action potential firing, thus increasing the stretch-sensitivity of the muscle spindle afferents. For an interactive animation created by Jan Kowalczewski at the University of Alberta, demonstrating spindle afferent responses to muscle stretch with and without gamma (fusimotor) action, go to: .

How does the central nervous system control gamma fusimotor neurons? It has been difficult to record from gamma motoneurons during normal movement because they have very small axons. Several theories have been proposed, based on recordings from spindle afferents.

- 1) *Alpha-gamma coactivation.* Here it is posited that gamma motoneurons are activated in parallel with alpha motoneurons to maintain the firing of spindle afferents when the extrafusal muscles shorten.
- 2) *Fusimotor set:* gamma motoneurons are activated according to the novelty or difficulty of a task. Whereas static gamma motoneurons are continuously active during routine movements such as locomotion, dynamic gamma motoneoruns tend to be activated more during difficult tasks, increasing Ia stretch-sensitivity.
- 3) *Fusimotor template of intended movement.* Static gamma activity is a "temporal template" of the expected shortening and lengthening of the receptor-bearing muscle. Dynamic gamma activity turns on and off abruptly, sensitizing spindle afferents to the onset of muscle lengthening and departures from the intended movement trajectory.

Stretch reflex

When a muscle is stretched, primary sensory fibers (Group Ia afferent neurons) of the muscle spindle respond to both changes in muscle length and velocity and transmit this activity to the spinal cord in the form of changes in the rate of action potentials. Likewise, secondary sensory fibers (Group II afferent neurons) respond to muscle length changes (but with a smaller velocity-sensitive component) and transmit this signal to the spinal cord. The Ia afferent signals are transmitted monosynaptically to many alpha motor neurons of the receptor-bearing muscle. The reflexly-evoked activity in the alpha motoneurons is then transmitted via their efferent axons to the extrafusal fibers of the muscle, which generate force and thereby resist the stretch. The Ia afferent signal is also transmitted polysynaptically through interneurons (Renshaw_cells) which inhibit alpha motoneurons of antagonist muscles, causing them to relax.

After stroke or spinal cord injury in humans, spastic hypertonus(spastic paresis or spatic paralysis) often develops, whereby the stretch reflex in flexor muscles of the arms and extensor muscles of the legs is overly sensitive. This results in abnormal postures, stiffness and contractures. Hypertonus(Hypertonia) may be the result of over-sensitivity of alpha motoneurons and interneurons to the Ia and II afferent signals.

PNF stretching, or proprioceptive neuromuscular facilitation, is a method of flexibility training that can reduce hypertonus, allowing muscles to relax and lengthen.

Development

It is also believed that muscle spindles play a critical role in sensorimotor development.

Neural adaptation

Neural adaptation or **sensory adaptation** is a change over time in the responsiveness of the sensory system to a constant stimulus. It is usually experienced as a change in the stimulus. For example, if one rests one's hand on a table, one immediately feels the table's surface on one's skin. Within a few seconds, however, one ceases to feel the table's surface. The sensory neurons stimulated by the table's surface respond immediately, but then respond less and less until they may not respond at all; this is neural adaptation.

Weight Training

Studies have shown that there is neural adaptation after as little as one weight training session. Strength gains are experienced by subjects without any increased muscle size. Muscle surface recordings using electromyographic (SEMG) techniques have found that early strength gains throughout training are associated with increased amplitude in SEMG activity. These findings along with various other theories explain increases in strength without increases in muscle mass. Other theories for increases in strength relating to neural adaptation include: agonist-antagonist muscle decreased co-activation, motor unit synchronization, and motor unit increased firing rates. Neural adaptations can be contributed to changes in V-waves and the Hoffmann's reflex. H-reflex can be used to assess the excitability of spinal α-motoneurons, whereas V-wave measure the magnitude of efferent motor output from α-motoneurons. Studies showed that after a 14 week resistance training regime that subjects expressed V-wave amplitude increases of ~50% and H-reflex amplitude increases of ~20%. This showed that neural adaptation accounts for changes to functional properties of the spinal cord circuitry in humans without affecting organization of the motor cortex.

Visual

Adaptation is considered to be the cause of perceptual phenomena like afterimages and the motion aftereffect. In the absence of fixational eye movements, visual perception may fade out or disappear due to neural adaptation. When an observers' visual stream adapts to a single direction of real motion, imagined motion can be perceived at various different speeds. If the imagined motion is in the same direction as that experienced during adaptation, imagined speed is slowed; when imagined motion is in the opposite direction, its speed is increased; when adaptation and imagined motions are orthogonal, imagined speed is unaffected. Studies using magnetoencephalography (MEG) have proven that subjects exposed to a repeated visual stimulus at brief intervals become attenuated to the stimulus in comparison to the initial stimulus. The results revealed that visual responses to the repeated compared with novel stimulus showed a significant reduction in both activation strength and peak latency but not in the duration of neural processing.

Pain

While large mechanosensory neurons such as type I/group Aß display adaptation, smaller type IV/group C nociceptive neurons do not. As a result, pain does not usually subside rapidly but persists for long periods of time; in contrast, one quickly stops receiving touch or sensory information if surroundings remain constant.

Rhythmic Behaviors

Short-Term Adaptations

Short term neural adaptations occur in the body during rhythmic activities. One of the most common activities when these neural adaptations are constantly happening is walking. As a person walks, the body constantly gathers information about the environment and the surroundings of the feet, and slightly adjusts the muscles in use according to the terrain. For example, walking uphill requires different muscles than walking on flat pavement. When the brain recognizes that the body is walking uphill, it makes neural adaptations that send more activity to muscles required for uphill walking. The rate of neural adaptation is affected by the area of the brain and by the similarity between sizes and shapes of previous stimuli. Adaptations in the inferior temporal gyrus are very dependent on previous stimuli being of similar size, and somewhat dependent on previous stimuli being of a similar shape. Adaptations in the Prefrontal Cortex are less dependent on previous stimuli being of similar size and shape.

Long-Term Adaptations

Some rhythmic movements, such as respiratory movements, are essential for survival. Because these movements must be used over the course of the entire lifetime, it is important for them to function optimally. Neural adaptation has been observed in these movements in response to training or altered external conditions. Animals have been shown to have reduced breathing rates in response to better fitness levels. Since breathing rates were not conscious changes made by the animal, it is presumed that neural adaptations occur for the body to maintain a slower breathing rate.

Transcranial Magnetic Stimulation

Transcranial magnetic stimulation (TMS) is an important technique in modern cognitive neuropsychology that is used to investigate the perceptual and behavioral effects of temporary interference of neural processing. Studies have shown that when a subject's visual cortex is disrupted by TMS, the subject views colorless flashes of light, or phosphenes. When a subjects' vision was subjected to the constant stimulus of a single color, neural adaptations occurred that made the subjects used to the color. Once this adaptation had occurred, TMS was used to disrupt the subjects' visual cortex again, and the flashes of light viewed by the subject were the same color as the constant stimulus before the disruption.

Drug Induced Neural Adaptation

Neural adaptation can occur for other than natural means. Antidepressant drugs, such as those that cause down regulation of β- adrenergic receptors, can cause rapid neural adaptations in the brain. By creating a quick adaptation in the regulation of these receptors, it is possible for drugs to reduce the effects of stress on those taking the medication.

Post-Injury Neural Adaptation

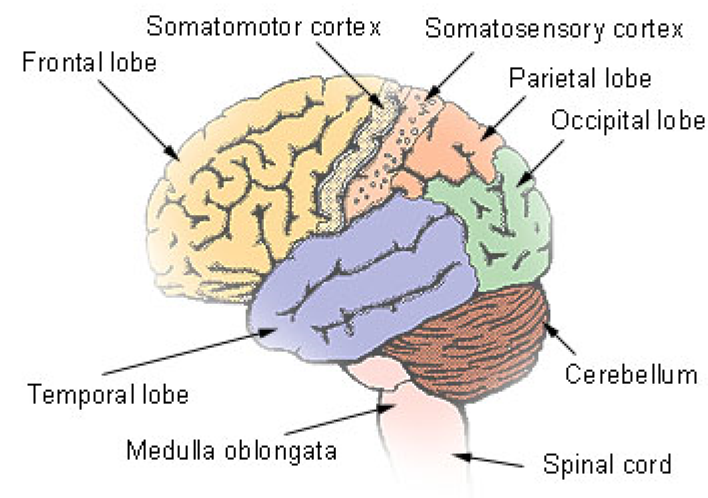
Studies in children with early childhood brain injuries have shown that neural adaptations slowly occur after the injury. Children with early injuries to the linguistics , spatial cognition and affective development areas of the brain showed deficits in those areas as compared to those without injury. Due to neural adaptations, however, by early school-age, considerable development to those areas was observed.

Current Research

Many universities are examining the effects of Neural Adaptation and how it can be used to improve current medical and rehabilitation techniques.

Chapter 11

Proprioception



The cerebellum is largely responsible for coordinating the unconscious aspects of proprioception.

Proprioception is the sense of the relative position of neighbouring parts of the body. Unlike the exteroceptive senses, by which we perceive the outside world, and interoceptive senses, by which we perceive the pain and movement of internal organs, proprioception is a third distinct sensory modality that provides feedback solely on the status of the body internally. It is the sense that indicates whether the body is moving with the required effort, as well as where the various parts of the body are located in relation to each other.

History of study

The position-movement sensation was originally described in 1557 by Julius Caesar Scaliger as a 'sense of locomotion'. Much later, in 1826, Charles Bell expounded the idea of a 'muscle sense' and this is credited with being one of the first physiologic feedback mechanisms. Bell's idea was that commands were being carried from the brain to the muscles, and that reports on the muscle's condition would be sent in the reverse direction. Later, in 1880, Henry Charlton Bastian suggested 'kinaesthesia' instead of 'muscle sense' on the basis that some of the afferent information (back to the brain) was coming from other structures including tendons, joints, and skin. In 1889, Alfred Goldscheider suggested a classification of kinaesthesia into 3 types: muscle, tendon, and articular sensitivity.

In 1906, Charles Scott Sherrington published a landmark work that introduced the terms 'proprioception', 'interoception', and 'exteroception'. The 'exteroceptors' are the organs responsible for information from outside the body such as the eyes, ears, mouth, and skin. The interoceptors then give information about the internal organs, while 'proprioception' is awareness of movement derived from muscular, tendon, and articular sources. Such a system of classification has kept physiologists and anatomists searching for specialised nerve endings that transmit data on joint capsule and muscle tension (such as muscle spindles and Pacini corpuscles).

Proprioception vs. kinesthesia

Kinesthesia is another term that is often used interchangeably with proprioception, though use of the term "kinesthesia" can place a greater emphasis on motion.

Some differentiate the kinesthetic sense from proprioception by excluding the sense of equilibrium or balance from kinesthesia. An inner ear infection, for example, might degrade the sense of balance. This would degrade the proprioceptive sense, but not the kinesthetic sense. The affected individual would be able to walk, but only by using the sense of sight to maintain balance; the person would be unable to walk with eyes closed.

Proprioception and kinesthesia are seen as interrelated and there is considerable disagreement regarding the definition of these terms. Some of this difficulty stems from Sherrington's original description of joint position sense (or the ability to determine exactly where a particular body part is in space) and kinesthesia (or the sensation that the body part has moved) under a more general heading of proprioception. Clinical aspects of proprioception are measured in tests that measure a subject's ability to detect an externally imposed passive movement, or the ability to reposition a joint to a predetermined position. Often it is assumed that the ability of one of these aspects will be related to another; however, experimental evidence suggests there is no strong relation between these two aspects. This suggests that while these components may well be related in a cognitive manner, they may in fact be physiologically separate.

Much of the foregoing work is dependent on the notion that proprioception is, in essence, a feedback mechanism; that is, the body moves (or is moved) and then the information about this is returned to the brain, whereby subsequent adjustments could be made. More recent work into the mechanism of ankle sprains suggests that the role of reflexes may be more limited due to their long latencies (even at the spinal cord level), as ankle sprain events occur in perhaps 100 ms or less. In accordance, a model has been proposed to include a 'feedforward' component of proprioception, whereby the subject will also have central information about the body's position prior to attaining it.

Kinesthesia is a key component in muscle memory and hand-eye coordination, and training can improve this sense. The ability to swing a golf club or to catch a ball requires a finely tuned sense of the position of the joints. This sense needs to become automatic through training to enable a person to concentrate on other aspects of performance, such as maintaining motivation or seeing where other people are.

Basis of proprioceptive sense

The initiation of proprioception is the activation of a proprioreceptor in the periphery. The proprioceptive sense is believed to be composed of information from sensory neurons located in the inner ear (motion and orientation) and in the stretch receptors located in the muscles and the joint-supporting ligaments (stance). There are specific nerve receptors for this form of perception termed "proprioreceptors," just as there are specific receptors for pressure, light, temperature, sound, and other sensory experiences. Proprioreceptors are sometimes known as adequate stimuli receptors.

Although it was known that finger kinesthesia relies on skin sensation, recent research has found that kinesthesia-based haptic perception relies strongly on the forces experienced during touch. This research allows the creation of "virtual", illusory haptic shapes with different perceived qualities.

Conscious and unconscious proprioception

In humans, a distinction is made between *conscious* proprioception and *unconscious* proprioception:

- Conscious proprioception is communicated by the posterior column-medial lemniscus pathway to the cerebrum.
- Unconscious proprioception is communicated primarily via the dorsal spinocerebellar tract, to the cerebellum.
- Such an unconscious reaction is seen in the human proprioceptive reflex. This remarkable proprioceptive reflex (Law of Righting), in the event that the body tilts in any direction, will cock the head back to level the eyes against the horizon. This is seen even in infants as soon as they gain control of their neck muscles. This control comes from the cerebellum, the part of the brain affecting balance.

Applications

Law enforcement

Proprioception is tested by American police officers using the field sobriety test, wherein the subject is required to touch his or her nose with eyes closed. People with normal proprioception may make an error of no more than 20 millimeters. People suffering from impaired proprioception (a symptom of moderate to severe alcohol intoxication) fail this test due to difficulty locating their limbs in space relative to their noses.

Diagnosis

There are several relatively specific tests of the subject's ability to propriorecept. These tests are used in the diagnosis of neurological disorders. They include the visual and tactile placing reflexes.

Learning new skills

Proprioception is what allows someone to learn to walk in complete darkness without losing balance. During the learning of any new skill, sport, or art, it is usually necessary to become familiar with some proprioceptive tasks specific to that activity. Without the appropriate integration of proprioceptive input, an artist would not be able to brush paint onto a canvas without looking at the hand as it moved the brush over the canvas; it would be impossible to drive an automobile because a motorist would not be able to steer or use the foot pedals while looking at the road ahead; a person could not touch type or perform ballet; and people would not even be able to walk without watching where they put their feet.

Oliver Sacks once reported the case of a young woman who lost her proprioception due to a viral infection of her spinal cord. At first she was not able to move properly at all or even control her tone of voice (as voice modulation is primarily proprioceptive). Later she relearned by using her sight (watching her feet) and inner ear only for movement while using hearing to judge voice modulation. She eventually acquired a stiff and slow movement and nearly normal speech, which is believed to be the best possible in the absence of this sense. She could not judge effort involved in picking up objects and would grip them painfully to be sure she did not drop them.

Training

The proprioceptive sense can be sharpened through study of many disciplines. Examples are the Feldenkrais method and the Alexander Technique. Juggling trains reaction time, spatial location, and efficient movement. Standing on a wobble board or balance board is often used to retrain or increase proprioception abilities, particularly as physical therapy for ankle or knee injuries. Standing on one leg (stork standing) and various other body-position challenges are also used in such disciplines as Yoga, Wing Chun and Tai Chi. Several studies have shown that the efficacy of these types of training is challenged by closing the eyes, because the eyes give invaluable feedback to establishing the moment-to-moment information of balance. There are even specific devices designed for proprioception training, such as the exercise ball, which works on balancing the abdominal and back muscles.

Impairment

It has been seen that temporary loss or impairment of proprioception may happen periodically during growth, mostly during adolescence. Growth that might also influence this would be large increases or drops in bodyweight/size due to fluctuations of fat (liposuction, rapid fat loss or gain) and/or muscle content (bodybuilding, anabolic steroids, catabolisis/starvation). It can also occur in those that gain new levels of flexibility, stretching, and contortion. A limb's being in a new range of motion never experienced (or at least, not for a long time since youth perhaps) can disrupt one's sense of location of that limb. Possible experiences include suddenly feeling that feet or legs are missing from one's mental self-image; needing to look down at one's limbs to be sure they are still there; and falling down while walking, especially when attention is focused upon something other than the act of walking.

Proprioception is occasionally impaired spontaneously, especially when one is tired. One's body may appear too large or too small, or parts of the body may appear distorted in size. Similar effects can sometimes occur during epilepsy or migraine auras. These effects are presumed to arise from abnormal stimulation of the part of the parietal cortex of the brain involved with integrating information from different parts of the body.

Proprioceptive illusions can also be induced, such as the Pinocchio illusion.

The proprioceptive sense is often unnoticed because humans will adapt to a continuously-present stimulus; this is called habituation, desensitization, or adaptation. The effect is that proprioceptive sensory impressions disappear, just as a scent can disappear over time. One practical advantage of this is that unnoticed actions or sensation continue in the background while an individual's attention can move to another concern. The Alexander Technique addresses these issues.

People that have a limb amputated may still have a confused sense of that limb existence on their body, known as phantom limb syndrome. Phantom sensations can occur as passive proprioceptive sensations of the limb's presence, or more active sensations such as perceived movement, pressure, pain, itching, or temperature. The etiology of the phantom limb phenomenon was disputed in 2006, but some consensus existed in favour of neurological (e.g., neural signal bleed across a preexisting sensory map, as posited by V.S. Ramachandran) over psychological explanations. Phantom sensations and phantom pain may also occur after the removal of body parts other than the limbs, such as after amputation of the breast, extraction of a tooth (phantom tooth pain), or removal of an eye (phantom eye syndrome).

Temporary impairment of proprioception has also been known to occur from an overdose of vitamin B6 (pyridoxine and pyridoxamine). Most of the impaired function returns to normal shortly after the intake of vitamins returns to normal. Impairment can also be caused by cytotoxic factors such as chemotherapy.

It has been proposed that even common tinnitus and the attendant hearing frequency-gaps masked by the perceived sounds may cause erroneous proprioceptive information to the balance and comprehension centers of the brain, precipitating mild confusion.

Proprioception is permanently impaired in patients that suffer from joint hypermobility or Ehlers-Danlos Syndrome (a genetic condition that results in weak connective tissue throughout the body). It can also be permanently impaired from viral infections as reported by Sacks. The catastrophic effect of major proprioceptive loss is reviewed by Robles-De-La-Torre (2006).

Chapter 12

Receptive Field

The **receptive field** of a sensory neuron is a region of space in which the presence of a stimulus will alter the firing of that neuron. Receptive fields have been identified for neurons of the auditory system, the somatosensory system, and the visual system.

The concept of receptive fields can be extended to further up the neural system; if many sensory receptors all form synapses with a single cell further up, they collectively form the receptive field of that cell. For example, the receptive field of a ganglion cell in the retina of the eye is composed of input from all of the photoreceptors which synapse with it, and a group of ganglion cells in turn forms the receptive field for a cell in the brain. This process is called convergence.

Auditory system

In the auditory system, receptive fields can be volumes in auditory space, or can be regions of auditory frequencies. Researchers rarely equate auditory receptive fields to particular regions of the sensory epithelium such as, in the case of mammals, hair cells in the cochlea.

Somatosensory system

In the somatosensory system, receptive fields are regions of the skin or of internal organs. Some types of mechanoreceptors have large receptive fields, while others have smaller ones.

Large receptive fields allow the cell to detect changes over a wider area, but lead to a less precise perception. Thus, the fingers, which require the ability to detect fine detail, have many, densely packed (up to 500 per cubic cm) mechanoreceptors with small receptive fields (around 10 square mm), while the back and legs, for example, have fewer receptors with large receptive fields. Receptors with large receptive fields usually have a "hot spot", an area within the receptive field (usually in the center, directly over the receptor) where stimulation produces the most intense response.

Tactile-sense-related cortical neurons have receptive fields on the skin that can be modified by experience or by injury to sensory nerves resulting in changes in the field's size and position. In general these neurons have relatively large receptive fields (much larger than those of dorsal root ganglion cells. However, the neurons are able to discriminate fine detail due to patterns of excitation and inhibition relative to the field which leads to spatial resolution.

Visual system

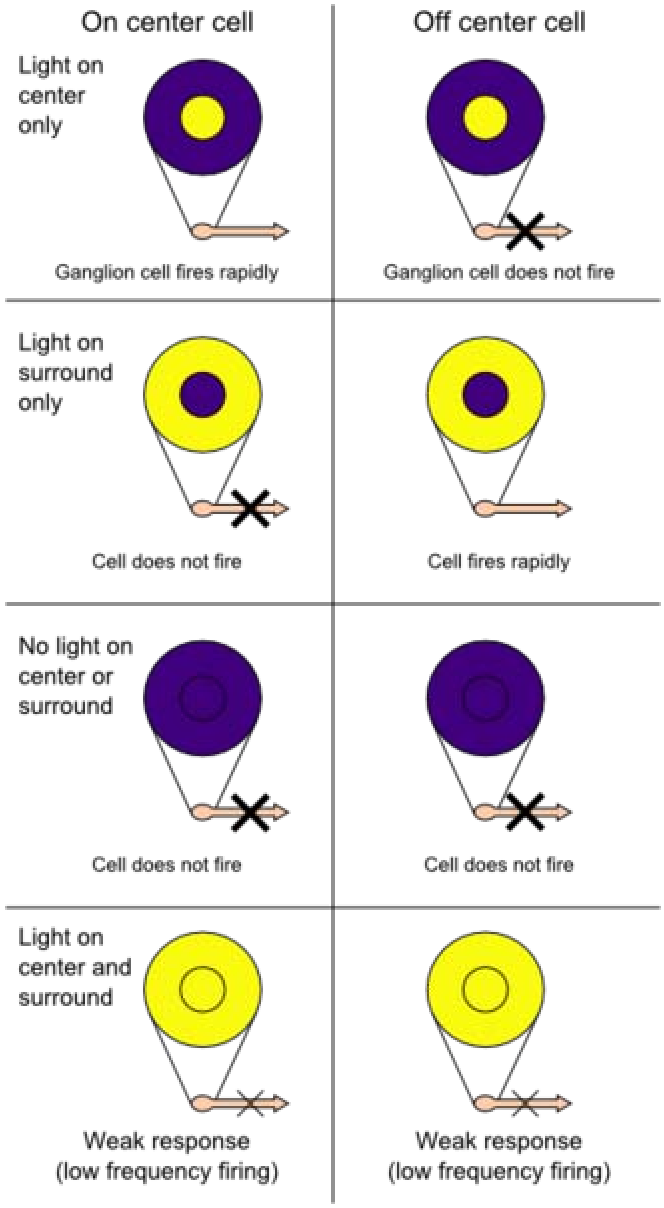
In the visual system, receptive fields are volumes in visual space. For example, the receptive field of a single photoreceptor is a cone-shaped volume comprising all the visual directions in which light will alter the firing of that cell. Its apex is located in the center of the lens and its base essentially at infinity in visual space. Traditionally, visual receptive fields were portrayed in two dimensions (e.g., as circles, squares, or rectangles), but these are simply slices, cut along the screen on which the researcher presented the stimulus, of the volume of space to which a particular cell will respond. In the case of binocular neurons in the visual cortex, receptive fields do not extend to optical infinity. Instead, they are restricted to a certain interval of distance from the animal, or from where the eyes are fixating.

The receptive field is often identified as the region of the retina where the action of light alters the firing of the neuron. In retinal ganglion cells (see below), this area of the retina would encompass all the photoreceptors, all the rods and cones from one eye that are connected to this particular ganglion cell via bipolar cells, horizontal cells, and amacrine cells. In binocular neurons in the visual cortex, it is necessary to specify the corresponding area in both retinas (one in each eye). Although these can be mapped separately in each retina by shutting one or the other eye, the full influence on the neuron's firing is revealed only when both eyes are open.

Hubel and Wiesel (e.g., Hubel, 1963) advanced the theory that receptive fields of cells at one level of the visual system are formed from input by cells at a lower level of the visual system. In this way, small, simple receptive fields could be combined to form large, complex receptive fields. Later theorists elaborated this simple, hierarchical arrangement by allowing cells at one level of the visual system to be influenced by feedback from higher levels.

Receptive fields have been mapped for all levels of the visual system from photoreceptors, to retinal ganglion cells, to lateral geniculate nucleus cells, to visual cortex cells, to extrastriate cortical cells. Studies based on perception do not give the full picture of the understanding of visual phenomena, so the electrophysiological tools must be used, as the retina, after all, is an outgrowth of the brain.

Retinal ganglion cells



On center and off center retinal ganglion cells respond oppositely to light in the center and surround of their receptive fields. A strong response means high frequency firing, a weak response is firing at a low frequency, and no response means no action potential is fired.

A computer emulation of “edge detection” using retinal receptive fields. On-centre and off-centre stimulation is shown in red and green respectively.

Each ganglion cell or optic nerve fiber bears a receptive field, increasing with intensifying light. In the largest field, the light had to be more intense at the periphery of the field than at the center, showing that some synaptic pathways are more preferred than others.

The organization of ganglion cells' receptive fields, composed of inputs from many rods and cones, provides a way of detecting contrast, and is used for detecting objects' edges. Each receptive field is arranged into a central disk, the "center", and a concentric ring, the "surround", each region responding oppositely to light. For example, light in the centre might increase the firing of a particular ganglion cell, whereas light in the surround would decrease the firing of that cell.

There are two types of bipolar cells: "on-center" and "off-center". An on-center cell is stimulated when the center of its receptive field is exposed to light, and is inhibited when the surround is exposed to light. Off-center cells have just the opposite reaction. On the edge between the two, in mammals, an on-off effect (i.e., discharging at switching on or off but not at a duration of either state) is present. Stimulation of the center of an on-center cell's receptive field produces *depolarization* and an increase in the firing of the ganglion cell, stimulation of the surround produces a *Hyperpolarization* and a decrease in the firing of the cell, and stimulation of both the center and surround produces only a mild response (due to mutual inhibition of center and surround). An off-center cell is stimulated by activation of the surround and inhibited by stimulation of the center (see figure).

Photoreceptors that are part of the receptive fields of more than one ganglion cell are able to excite or inhibit postsynaptic neurons because they release the neurotransmitter glutamate at their synapses, which can act to depolarize or to hyperpolarize a cell, depending on the ion channels it opens.

The center-surround receptive field organization allows ganglion cells to transmit information not merely about whether photoreceptor cells are exposed to light, but also about the differences in firing rates of cells in the center and surround. This allows them to transmit information about contrast. The size of the receptive field governs the spatial frequency of the information: small receptive fields are stimulated by high spatial frequencies, fine detail; large receptive fields are stimulated by low spatial frequencies, coarse detail. Retinal ganglion cell receptive fields convey information about discontinuities in the distribution of light falling on the retina; these often specify the edges of objects. In dark adaptation, the peripheral opposite activity zone becomes inactive, but, since it is a diminishing of inhibition between center and periphery, the active field can actually increase, allowing more area for summation.

The receptive field tends to favor movement (such as a light or dark spot moving over the field, as in center-to-periphery (or vice versa)), as well as contours (due to their nonuniformity in the receptive fields). The center of the visual field has as much diameter as its dendrite spread, so the periphery is founded by amacrine cells connecting a wide area of bipolars to the ganglion. These amacrine cells can also inhibit signals of the periphery from being transmitted to the ganglion, thus rendering it on-center, off-periphery. In the rabbit, one direction, the "preferred," of a moving patch of light will excite a ganglion cell, whereas the opposite ("null") direction will not, also inhibiting spontaneous activity. Thus, there may be a linear nature of photoreceptors, one inhibiting its following neighbor when moving in the null direction, but arriving too late at the adjacent cell when traveling in the preferred direction.

Lateral geniculate nucleus

Further along in the visual system, groups of ganglion cells form the receptive fields of cells in the lateral geniculate nucleus. Receptive fields are similar to those of ganglion cells, with an antagonistic center-surround system and cells that are either on- or off center.

Visual cortex

Receptive fields of cells in the visual cortex are larger and have more-complex stimulus requirements than retinal ganglion cells or lateral geniculate nucleus cells. Hubel and Wiesel (e.g., Hubel, 1963) classified receptive fields of cells in the visual cortex into simple cells, complex cells, and hypercomplex cells. Simple cell receptive fields are elongated, for example with an excitatory central oval, and an inhibitory surrounding region, or approximately rectangular, with one long side being excitatory and the other being inhibitory. Images for these receptive fields need to have a particular orientation in order to excite the cell. For complex-cell receptive fields, a correctly oriented bar of light might need to move in a particular direction in order to excite the cell. For hypercomplex receptive fields, the bar might also need to be of a particular length.

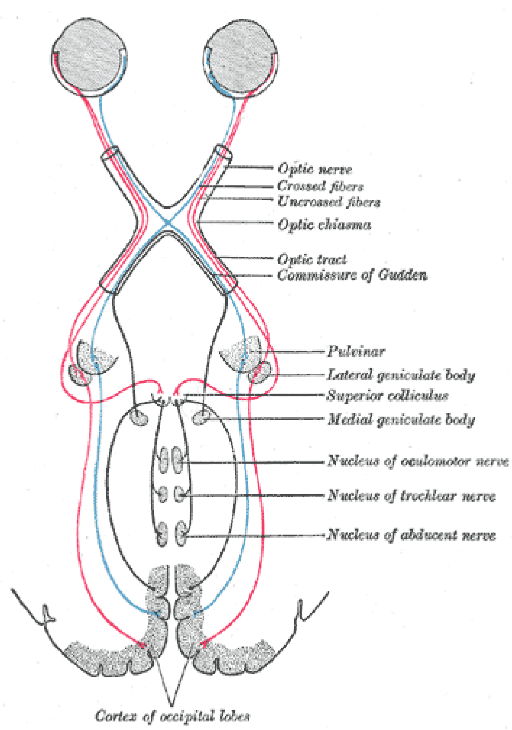
Extrastriate visual areas

In extrastriate visual areas, cells can have very large receptive fields requiring very complex images to excite the cell. For example in the inferotemporal cortex, receptive fields cross the midline of visual space and require images such as radial gratings or hands. It is also believed that in the fusiform face area, images of faces excite the cortex more than other images. This property was one of the earliest major results obtained through fMRI (Kanwisher, McDermott and Chun, 1997); the finding was confirmed later at the neuronal level (Tsao, Freiwald, Tootell and Livingstone, 2006). In a similar vein, people have looked for other category-specific areas; some recent research for example suggests the parahippocampal place area might be somewhat specialised for buildings. However, more recent research has suggested that the fusiform face area is specialised not just for faces, but also for any discrete, within-category discrimination.

Chapter 13

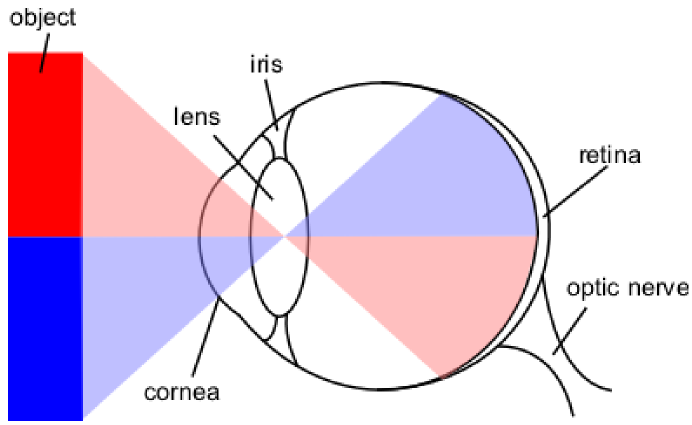
Visual System

The **visual system** is the part of the central nervous system which enables organisms to process visual detail, as well as enabling several non-image forming photoresponse functions. It interprets information from visible light to build a representation of the surrounding world. The visual system accomplishes a number of complex tasks, including the reception of light and the formation of monocular representations; the construction of a binocular perception from a pair of two dimensional projections; the identification and categorization of visual objects; assessing distances to and between objects; and guiding body movements in relation to visual objects. The psychological manifestation of visual information is known as visual perception, a lack of which is called blindness. Non-image forming visual functions, independent of visual perception, include the pupillary light reflex (PLR) and circadian photoentrainment.



The visual system includes the eyes, the connecting pathways through to the visual cortex and other parts of the brain. The illustration shows the mammalian system.

Introduction



Optical layout of the eye

Here we, mostly describes the visual system of mammals, although other "higher" animals have similar visual systems. In this case, the visual system consists of:

- The eye, especially the retina
- The optic nerve
- The optic chiasma
- The optic tract
- The lateral geniculate body
- The optic radiation
- The visual cortex
- The visual association cortex.

Different species are able to see different parts of the light spectrum; for example, bees can see into the ultraviolet, while pit vipers can accurately target prey with their pit organs, which are sensitive to infrared radiation.

History

In the second half of the 19th century, many motifs of the nervous system were identified such as the neuron doctrine and brain localisation, which related to the neuron being the basic unit of the nervous system and functional localisation in the brain, respectively. These would become tenets of the fledgling neuroscience and would support further understanding of the visual system.

The notion that the cerebral cortex is divided into functionally distinct cortices now known to be responsible for capacities such as touch (somatosensory cortex), movement (motor cortex), and vision (visual cortex), was first proposed by Franz Joseph Gall in 1810. Evidence for functionally distinct areas of the brain (and, specifically, of the cerebral cortex) mounted throughout the 19th century with discoveries by Paul Broca of the language center (1861), and Gustav Fritsch and Edouard Hitzig of the motor cortex (1871). Based on selective damage to parts of the brain and the functional effects this would produce (lesion studies), David Ferrier proposed that visual function was localised to the parietal lobe of the brain in 1876. In 1881, Hermann Munk more accurately located vision in the occipital lobe, where the primary visual cortex is now known to be.

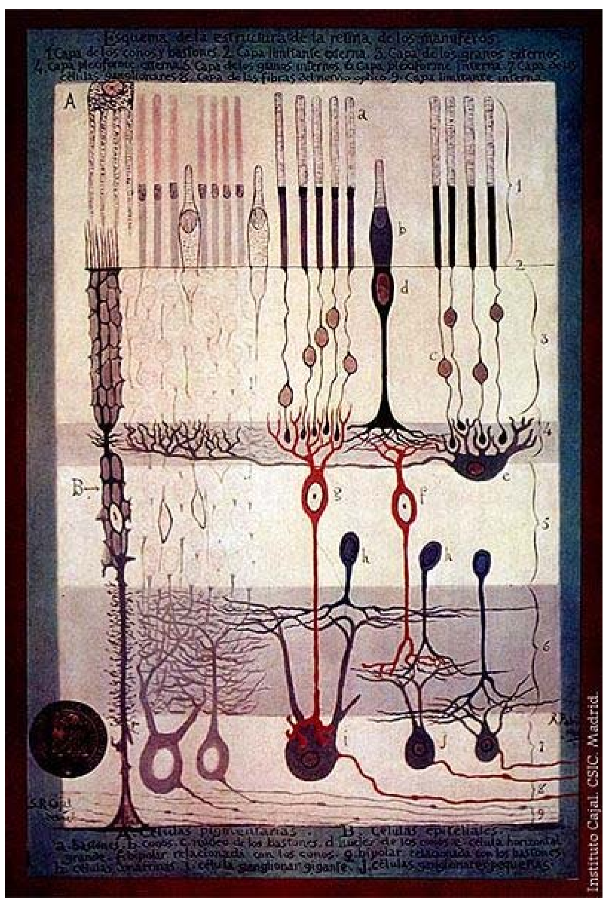
Biology of the visual system

Eye

The eye is a complex biological device. The functioning of a camera is often compared with the workings of the eye, mostly since both focus light from external objects in the field of view onto a light-sensitive medium. In the case of the camera, this medium is film or an electronic sensor; in the case of the eye, it is an array of visual receptors. With this simple geometrical similarity, based on the laws of optics, the eye functions as a transducer, as does a CCD camera.

Light entering the eye is refracted as it passes through the cornea. It then passes through the pupil (controlled by the iris) and is further refracted by the lens. The cornea and lens act together as a compound lens to project an inverted image onto the retina.

Retina



S. Ramón y Cajal, *Structure of the Mammalian Retina, 1900*

The retina consists of a large number of photoreceptor cells which contain particular protein molecules called opsins. In humans, two types of opsins are involved in conscious vision: rod opsins and cone opsins. (A third type, melanopsin in some of the retinal ganglion cells (RGC), part of the body clock mechanism, is probably not involved in conscious vision, as these RGC do not project to the lateral geniculate nucleus (LGN) but to the pretectal olivary nucleus (PON).) An opsin absorbs a photon (a particle of light) and transmits a signal to the cell through a signal transduction pathway, resulting in hyperpolarization of the photoreceptor.

Rods and cones differ in function. Rods are found primarily in the periphery of the retina and are used to see at low levels of light. Cones are found primarily in the center (or fovea) of the retina. There are three types of cones that differ in the wavelengths of light they absorb; they are usually called short or blue, middle or green, and long or red. Cones are used primarily to distinguish color and other features of the visual world at normal levels of light.

In the retina, the photoreceptors synapse directly onto bipolar cells, which in turn synapse onto ganglion cells of the outermost layer, which will then conduct action potentials to the brain. A significant amount of visual processing arises from the patterns of communication between neurons in the retina. About 130 million photoreceptors absorb light, yet roughly 1.2 million axons of ganglion cells transmit information from the retina to the brain. The processing in the retina includes the formation of center-surround receptive fields of bipolar and ganglion cells in the retina, as well as convergence and divergence from photoreceptor to bipolar cell. In addition, other neurons in the retina, particularly horizontal and amacrine cells, transmit information laterally (from a neuron in one layer to an adjacent neuron in the same layer), resulting in more complex receptive fields that can be either indifferent to color and sensitive to motion or sensitive to color and indifferent to motion. **Mechanism of generating visual signals**: The retina adapts to its change in light through the use of the rods. In the dark, the retinal has a bent shape called cis-retinal. When light is present, the retinal changes to a straight form called trans-retinal and breaks away from the opsin. This is called bleaching because the purified rhodopsin changes from violet to colorless in the light. In the dark, the rhodopsin absorbs no light therefore releasing glutamate cells which inhibit the bipolar cell. This inhibits the release of neurotransmitters to the ganglion cell. In the light, glutamate secretion ceases which no longer inhibits the bipolar cell from releasing neurotransmitters to the ganglion cell and therefore an image can be detected.

The final result of all this processing is five different populations of ganglion cells that send visual (image-forming and non-image-forming) information to the brain:

1. M cells, with large center-surround receptive fields that are sensitive to depth, indifferent to color, and rapidly adapt to a stimulus;
2. P cells, with smaller center-surround receptive fields that are sensitive to color and shape;
3. K cells, with very large center-only receptive fields that are sensitive to color and indifferent to shape or depth;

4. another population that is intrinsically photosensitive; and
5. a final population that is used for eye movements.

A 2006 University of Pennsylvania study calculated the approximate bandwidth of human retinas to be about 8960 kilobits per second, whereas guinea pig retinas transfer at about 875 kilobits.

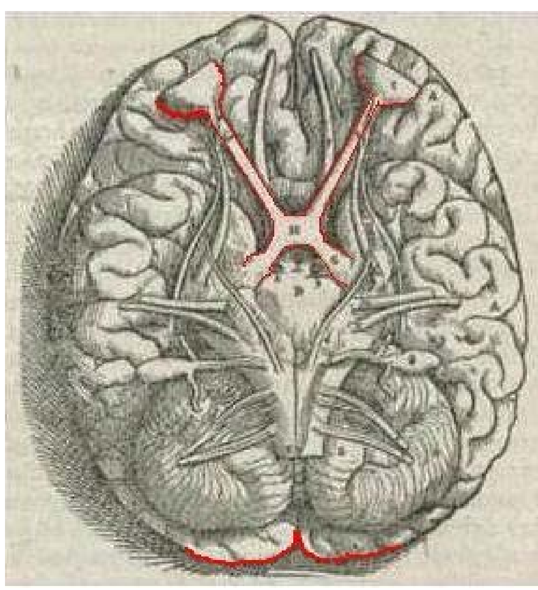
In 2007 Zaidi and co-researchers on both sides of the Atlantic studying patients without rods and cones, discovered that the novel photoreceptive ganglion cell in humans also has a role in conscious and unconscious visual perception. The peak spectral sensitivity was 481 nm. This shows that there are two pathways for sight in the retina – one based on classic photoreceptors (rods and cones) and the other, newly discovered, based on photoreceptive ganglion cells which act as rudimentary visual brightness detectors.

Photochemistry

In the visual system, **retinal**, technically called *retinene*$_1$ or "retinaldehyde", is a light-sensitive retinene molecule found in the rods and cones of the retina. Retinal is the fundamental structure involved in the transduction of light into visual signals, i.e. nerve impulses in the ocular system of the central nervous system. In the presence of light, the retinal molecule changes configuration and as a result a nerve impulse is generated.

Fibers to thalamus

Optic nerve



Information flow from the eyes (top), crossing at the optic chiasma, joining left and right eye information in the optic tract, and layering left and right visual stimuli in the lateral geniculate nucleus. V1 in red at bottom of image. (1543 image from Andreas Vesalius' *Fabrica*)

The information about the image via the eye is transmitted to the brain along the optic nerve. Different populations of ganglion cells in the retina send information to the brain through the optic nerve. About 90% of the axons in the optic nerve go to the lateral geniculate nucleus in the thalamus. These axons originate from the M, P, and K ganglion cells in the retina, see above. This parallel processing is important for reconstructing the visual world; each type of information will go through a different route to perception. Another population sends information to the superior colliculus in the midbrain, which assists in controlling eye movements (saccades) as well as other motor responses.

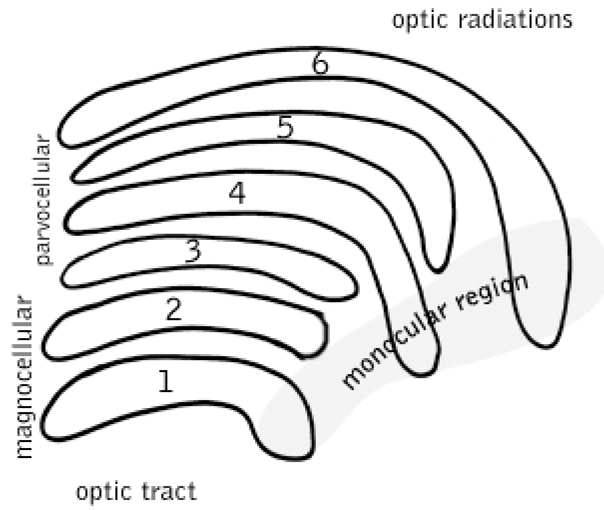
A final population of photosensitive ganglion cells, containing melanopsin, sends information via the retinohypothalamic tract (RHT) to the pretectum (pupillary reflex), to several structures involved in the control of circadian rhythms and sleep such as the suprachiasmatic nucleus (SCN, the biological clock), and to the ventrolateral preoptic nucleus (VLPO, a region involved in sleep regulation). A recently discovered role for photoreceptive ganglion cells is that they mediate conscious and unconscious vision – acting as rudimentary visual brightness detectors as shown in rodless coneless eyes.

Optic chiasm

The optic nerves from both eyes meet and cross at the optic chiasm, at the base of the hypothalamus of the brain. At this point the information coming from both eyes is combined and then splits according to the visual field. The corresponding halves of the field of view (right and left) are sent to the left and right halves of the brain, respectively, to be processed. That is, the right side of primary visual cortex deals with the left half of the *field of view* from both eyes, and similarly for the left brain. A small region in the center of the field of view is processed redundantly by both halves of the brain.

Optic tract

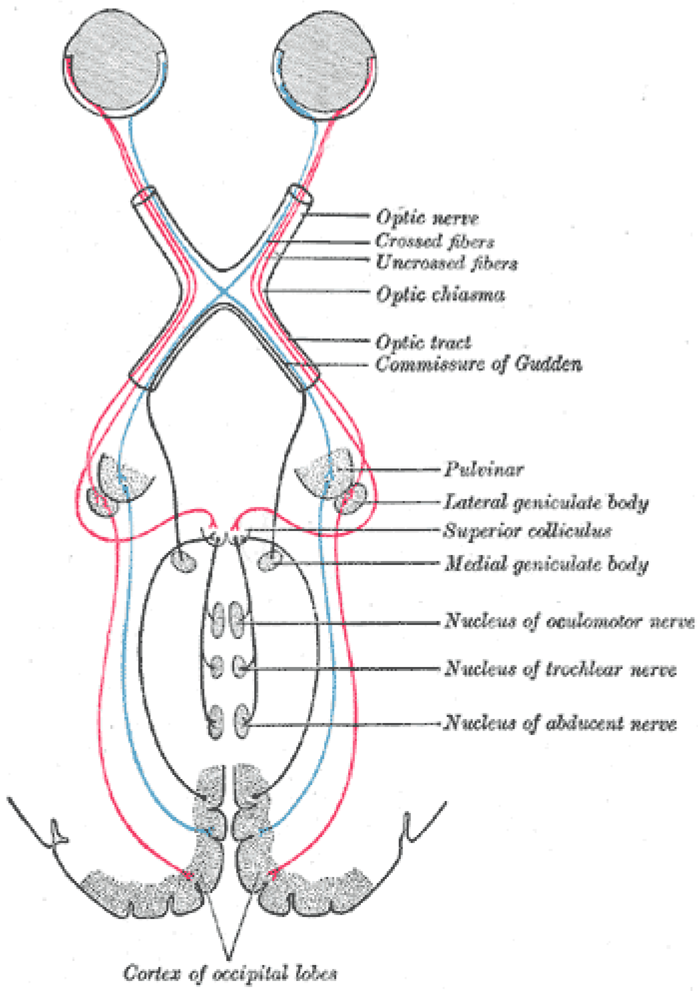
Information from the right *visual field* (now on the left side of the brain) travels in the left optic tract. Information from the left *visual field* travels in the right optic tract. Each optic tract terminates in the lateral geniculate nucleus (LGN) in the thalamus.



Six layers in the LGN

Lateral geniculate nucleus

The **lateral geniculate nucleus** (LGN) is a sensory relay nucleus in the thalamus of the brain. The LGN consists of six layers in humans and other primates starting from catarhinians, including cercopithecidae and apes. Layers 1, 4, and 6 correspond to information from the contralateral (crossed) fibers of the nasal visual field; layers 2, 3, and 5 correspond to information from the ipsilateral (uncrossed) fibers of the temporal visual field. Layer one (1) contains M cells which correspond to the M (magnocellular) cells of the optic nerve of the opposite eye and are concerned with depth or motion. Layers four and six (4 & 6) of the LGN also connect to the opposite eye, but to the P cells (color and edges) of the optic nerve. By contrast, layers two, three and five (2, 3, & 5) of the LGN connect to the M cells and P (parvocellular) cells of the optic nerve for the same side of the brain as its respective LGN. Spread out, the six layers of the LGN are the area of a credit card and about three times its thickness. The LGN is rolled up into two ellipsoids about the size and shape of two small birds' eggs. In between the six layers are smaller cells that receive information from the K cells (color) in the retina. The neurons of the LGN then relay the visual image to the primary visual cortex (V1) which is located at the back of the brain (caudal end) in the occipital lobe in and close to the calcarine sulcus The LGN is not just a simple relay station but its also a center for processing; it reecieves reciprocal input from the cortical and subcortical andreciprocal innervation from the visual cortex.



Scheme showing central connections of the optic nerves and optic tracts

Optic radiation

The **optic radiations**, one on each side of the brain, carry information from the thalamic lateral geniculate nucleus to layer 4 of the visual cortex. The P layer neurons of the LGN relay to V1 layer 4C β. The M layer neurons relay to V1 layer 4C α. The K layer neurons in the LGN relay to large neurons called blobs in layers 2 and 3 of V1.

There is a direct correspondence from an angular position in the field of view of the eye, all the way through the optic tract to a nerve position in V1. At this juncture in V1, the image path ceases to be straightforward; there is more cross-connection within the visual cortex.

Visual cortex

Visual cortex: V1, V2, V3, V4, V5 (also called MT)

The visual cortex is the largest system in the human brain and is responsible for processing the visual image. It lies at the rear of the brain (highlighted in the image), above the cerebellum. The region that receives information directly from the LGN is called the primary visual cortex, (also called V1 and striate cortex). Visual information then flows through a cortical hierarchy. These areas include V2, V3, V4 and area V5/MT (the exact connectivity depends on the species of the animal). These secondary visual areas (collectively termed the extrastriate visual cortex) process a wide variety of visual primitives. Neurons in V1 and V2 respond selectively to bars of specific orientations, or combinations of bars. These are believed to support edge and corner detection. Similarly, basic information about color and motion is processed here.

Visual association cortex

As visual information passes forward through the visual hierarchy, the complexity of the neural representations increase. Whereas a V1 neuron may respond selectively to a line segment of a particular orientation in a particular retinotopic location, neurons in the lateral occipital complex respond selectively to complete object (e.g., a figure drawing), and neurons in visual association cortex may respond selectively to human faces, or to a particular object.

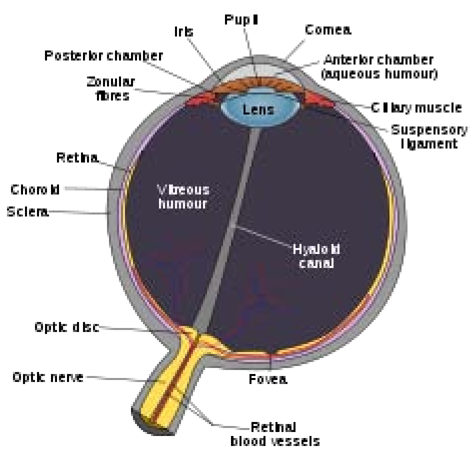
Along with this increasing complexity of neural representation may come a level of specialization of processing into two distinct pathways: the dorsal stream and the ventral stream (the Two Streams hypothesis, first proposed by Ungerleider and Mishkin in 1982). The dorsal stream, commonly referred to as the "where" stream, is involved in spatial attention (covert and overt), and communicates with regions that control eye movements and hand movements. More recently, this area has been called the "how" stream to emphasize its role in guiding behaviors to spatial locations. The ventral stream, commonly referred as the "what" stream, is involved in the recognition, identification and categorization of visual stimuli.

However, there is still much debate about the degree of specialization within these two pathways, since they are in fact heavily interconnected.

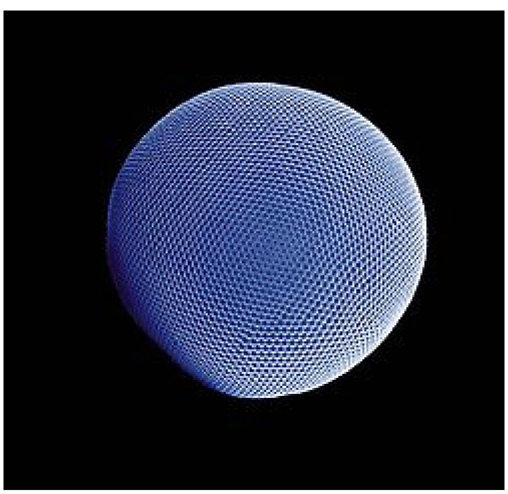
Chapter 14

Eye

Eye



Schematic diagram of the vertebrate eye.



Compound eye of Antarctic krill

Eyes are organs that detect light, and convert it to electro-chemical impulses in neurons. The simplest photoreceptors in conscious vision connect light to movement. In higher organisms the eye is a complex optical system which collects light from the surrounding environment; regulates its intensity through a diaphragm; focuses it through an adjustable assembly of lenses to form an image; converts this image into a set of electrical signals; and transmits these signals to the brain, through complex neural pathways that connect the eye, via the optic nerve, to the visual cortex and other areas of the brain. Eyes with resolving power have come in ten fundamentally different forms, and 96% of animal species possess a complex optical system. Image-resolving eyes are present in molluscs, chordates and arthropods.

The simplest "eyes", such as those in microorganisms, do nothing but detect whether the surroundings are light or dark, which is sufficient for the entrainment of circadian rhythms. From more complex eyes, retinal photosensitive ganglion cells send signals along the retinohypothalamic tract to the suprachiasmatic nuclei to effect circadian adjustment.

Overview

Eye of the wisent, the European bison

Complex eyes can distinguish shapes and colours. The visual fields of many organisms, especially predators, involve large areas of binocular vision to improve depth perception; in other organisms, eyes are located so as to maximize the field of view, such as in rabbits and horses, which have monocular vision.

The first proto-eyes evolved among animals 600 million years ago, about the time of the Cambrian explosion. The last common ancestor of animals possessed the biochemical toolkit necessary for vision, and more advanced eyes have evolved in 96% of animal species in six of the thirty-plus main phyla. In most vertebrates and some molluscs, the eye works by allowing light to enter and project onto a light-sensitive panel of cells, known as the retina, at the rear of the eye. The cone cells (for colour) and the rod cells (for low-light contrasts) in the retina detect and convert light into neural signals for vision. The visual signals are then transmitted to the brain via the optic nerve. Such eyes are typically roughly spherical, filled with a transparent gel-like substance called the vitreous humour, with a focusing lens and often an iris; the relaxing or tightening of the muscles around the iris change the size of the pupil, thereby regulating the amount of light that enters the eye, and reducing aberrations when there is enough light.

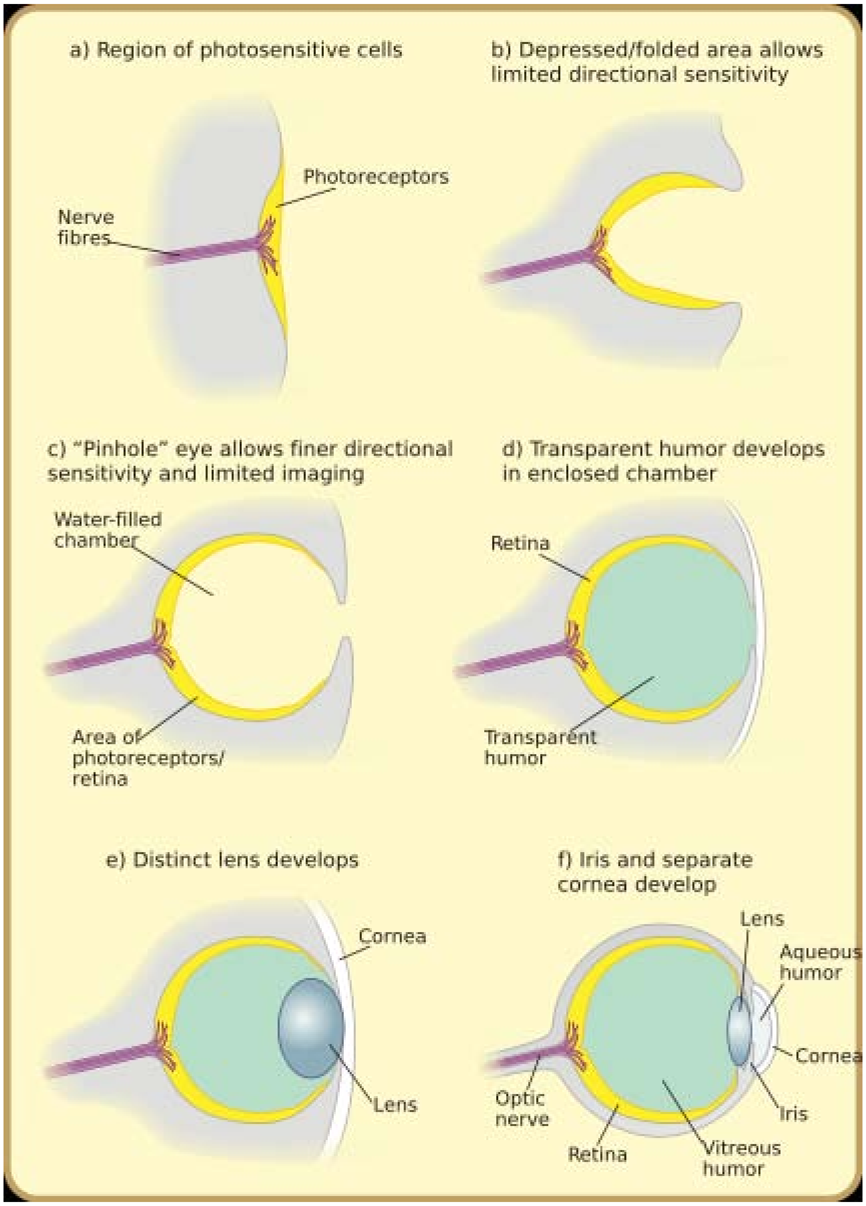
The eyes of most cephalopods, fish, amphibians and snakes have fixed lens shapes, and focusing vision is achieved by telescoping the lens—similar to how a camera focuses.

Compound eyes are found among the arthropods and are composed of many simple facets which, depending on the details of anatomy, may give either a single pixelated image or multiple images, per eye. Each sensor has its own lens and photosensitive cell(s). Some eyes have up to 28,000 such sensors, which are arranged hexagonally, and which can give a full 360-degree field of vision. Compound eyes are very sensitive to motion. Some arthropods, including many Strepsiptera, have compound eyes of only a few facets, each with a retina capable of creating an image, creating vision. With each eye viewing a different thing, a fused image from all the eyes is produced in the brain, providing very different, high-resolution images.

Possessing detailed hyperspectral colour vision, the Mantis shrimp has been reported to have the world's most complex colour vision system. Trilobites, which are now extinct, had unique compound eyes. They used clear calcite crystals to form the lenses of their eyes. In this, they differ from most other arthropods, which have soft eyes. The number of lenses in such an eye varied, however: some trilobites had only one, and some had thousands of lenses in one eye.

In contrast to compound eyes, simple eyes are those that have a single lens. For example, jumping spiders have a large pair of simple eyes with a narrow field of view, supported by an array of other, smaller eyes for peripheral vision. Some insect larvae, like caterpillars, have a different type of simple eye (stemmata) which gives a rough image. Some of the simplest eyes, called ocelli, can be found in animals like some of the snails, which cannot actually "see" in the normal sense. They do have photosensitive cells, but no lens and no other means of projecting an image onto these cells. They can distinguish between light and dark, but no more. This enables snails to keep out of direct sunlight. In organisms dwelling near deep-sea vents, compound eyes have been secondarily simplified and adapted to spot the infra-red light produced by the hot vents–in this way the bearers can spot hot springs and avoid being boiled alive.

Evolution



Evolution of the eye

Photoreception is phylogenetically very old, with various theories of phylogenesis. The common origin (monophyly) of all animal eyes is now widely accepted as fact. This is based upon the shared anatomical and genetic features of all eyes; that is, all modern eyes, varied as they are, have their origins in a proto-eye believed to have evolved some 540 million years ago. The majority of the advancements in early eyes are believed to have taken only a few million years to develop, since the first predator to gain true imaging would have touched off an "arms race". Prey animals and competing predators alike would be at a distinct disadvantage without such capabilities and would be less likely to survive and reproduce. Hence multiple eye types and subtypes developed in parallel.

Eyes in various animals show adaption to their requirements. For example, birds of prey have much greater visual acuity than humans, and some can see ultraviolet light. The different forms of eye in, for example, vertebrates and mollusks are often cited as examples of parallel evolution, despite their distant common ancestry.

The very earliest "eyes", called eyespots, were simple patches of photoreceptor protein in unicellular animals. In multicellular beings, multicellular eyespots evolved, physically similar to the receptor patches for taste and smell. These eyespots could only sense ambient brightness: they could distinguish light and dark, but not the direction of the lightsource.

Through gradual change, as the eyespot depressed into a shallow "cup" shape, the ability to slightly discriminate directional brightness was achieved by using the angle at which the light hit certain cells to identify the source. The pit deepened over time, the opening diminished in size, and the number of photoreceptor cells increased, forming an effective pinhole camera that was capable of dimly distinguishing shapes.

The thin overgrowth of transparent cells over the eye's aperture, originally formed to prevent damage to the eyespot, allowed the segregated contents of the eye chamber to specialize into a transparent humour that optimized color filtering, blocked harmful radiation, improved the eye's refractive index, and allowed functionality outside of water. The transparent protective cells eventually split into two layers, with circulatory fluid in between that allowed wider viewing angles and greater imaging resolution, and the thickness of the transparent layer gradually increased, in most species with the transparent crystallin protein.

The gap between tissue layers naturally formed a bioconvex shape, an optimally ideal structure for a normal refractive index. Independently, a transparent layer and a nontransparent layer split forward from the lens: the cornea and iris. Separation of the forward layer again formed a humour, the aqueous humour. This increased refractive power and again eased circulatory problems. Formation of a nontransparent ring allowed more blood vessels, more circulation, and larger eye sizes.

Types of eye

There are ten different eye layouts—indeed every way of capturing an optical image commonly used by man, with the exceptions of zoom and Fresnel lenses. Eye types can be categorized into "simple eyes", with one concave photoreceptive surface, and "compound eyes", which comprise a number of individual lenses laid out on a convex surface. Note that "simple" does not imply a reduced level of complexity or acuity.

Indeed, any eye type can be adapted for almost any behaviour or environment. The only limitations specific to eye types are that of resolution—the physics of compound eyes prevents them from achieving a resolution better than 1°. Also, superposition eyes can achieve greater sensitivity than apposition eyes, so are better suited to dark-dwelling creatures. Eyes also fall into two groups on the basis of their photoreceptor's cellular construction, with the photoreceptor cells either being cilliated (as in the vertebrates) or rhabdomeric. These two groups are not monophyletic; the cnidaria also possess cilliated cells, and some annelids possess both.

Non-compound eyes

Simple eyes are rather ubiquitous, and lens-bearing eyes have evolved at least seven times in vertebrates, cephalopods, annelids, crustacea and cubozoa.

Pit eyes

Pit eyes, also known as stemma, are eye-spots which may be set into a pit to reduce the angles of light that enters and affects the eyespot, to allow the organism to deduce the angle of incoming light. Found in about 85% of phyla, these basic forms were probably the precursors to more advanced types of "simple eye". They are small, comprising up to about 100 cells covering about 100 µm. The directionality can be improved by reducing the size of the aperture, by incorporating a reflective layer behind the receptor cells, or by filling the pit with a refractile material.

Pit vipers have developed pits that function as eyes by sensing thermal infra-red radiation, in addition to their optical wavelength eyes like those of other vertebrates.

Spherical lensed eye

The resolution of pit eyes can be greatly improved by incorporating a material with a higher refractive index to form a lens, which may greatly reduce the blur radius encountered—hence increasing the resolution obtainable. The most basic form, seen in some gastropods and annelids, consists of a lens of one refractive index. A far sharper image can be obtained using materials with a high refractive index, decreasing to the edges; this decreases the focal length and thus allows a sharp image to form on the retina. This also allows a larger aperture for a given sharpness of image, allowing more light to enter the lens; and a flatter lens, reducing spherical aberration. Such an inhomogeneous lens is necessary in order for the focal length to drop from about 4 times the lens radius, to 2.5 radii.

Heterogeneous eyes have evolved at least eight times: four or more times in gastropods, once in the copepods, once in the annelids and once in the cephalopods. No aquatic organisms possess homogeneous lenses; presumably the evolutionary pressure for a heterogeneous lens is great enough for this stage to be quickly "outgrown".

This eye creates an image that is sharp enough that motion of the eye can cause significant blurring. To minimize the effect of eye motion while the animal moves, most such eyes have stabilizing eye muscles.

The ocelli of insects bear a simple lens, but their focal point always lies behind the retina; consequently they can never form a sharp image. This capitulates the function of the eye. Ocelli (pit-type eyes of arthropods) blur the image across the whole retina, and are consequently excellent at responding to rapid changes in light intensity across the whole visual field; this fast response is further accelerated by the large nerve bundles which rush the information to the brain. Focusing the image would also cause the sun's image to be focused on a few receptors, with the possibility of damage under the intense light; shielding the receptors would block out some light and thus reduce their sensitivity. This fast response has led to suggestions that the ocelli of insects are used mainly in flight, because they can be used to detect sudden changes in which way is up (because light, especially UV light which is absorbed by vegetation, usually comes from above).

Multiple lenses

Some marine organisms bear more than one lens; for instance the copepod *Pontella* has three. The outer has a parabolic surface, countering the effects of spherical aberration while allowing a sharp image to be formed. Another copepod, *Copilia*'s eyes have two lenses, arranged like those in a telescope. Such arrangements are rare and poorly understood, but represent an interesting alternative construction. An interesting use of multiple lenses is seen in some hunters such as eagles and jumping spiders, which have a refractive cornea (discussed next): these have a negative lens, enlarging the observed image by up to 50% over the receptor cells, thus increasing their optical resolution.

Refractive cornea

In the eyes of most mammals, birds, reptiles, and most other terrestrial vertebrates (along with spiders and some insect larvae) the vitreous fluid has a higher refractive index than the air. In general, the lens is not spherical. Spherical lenses produce spherical aberration. In refractive corneas, the lens tissue is corrected with inhomogeneous lens material, or with an aspheric shape. Flattening the lens has a disadvantage; the quality of vision is diminished away from the main line of focus. Thus, animals that have evolved with a wide field-of-view often have eyes that make use of an inhomogeneous lens.

As mentioned above, a refractive cornea is only useful out of water; in water, there is little difference in refractive index between the vitreous fluid and the surrounding water. Hence creatures that have returned to the water—-penguins and seals, for example---lose their highly curved cornea and return to lens-based vision. An alternative solution, borne by some divers, is to have a very strongly focusing cornea.

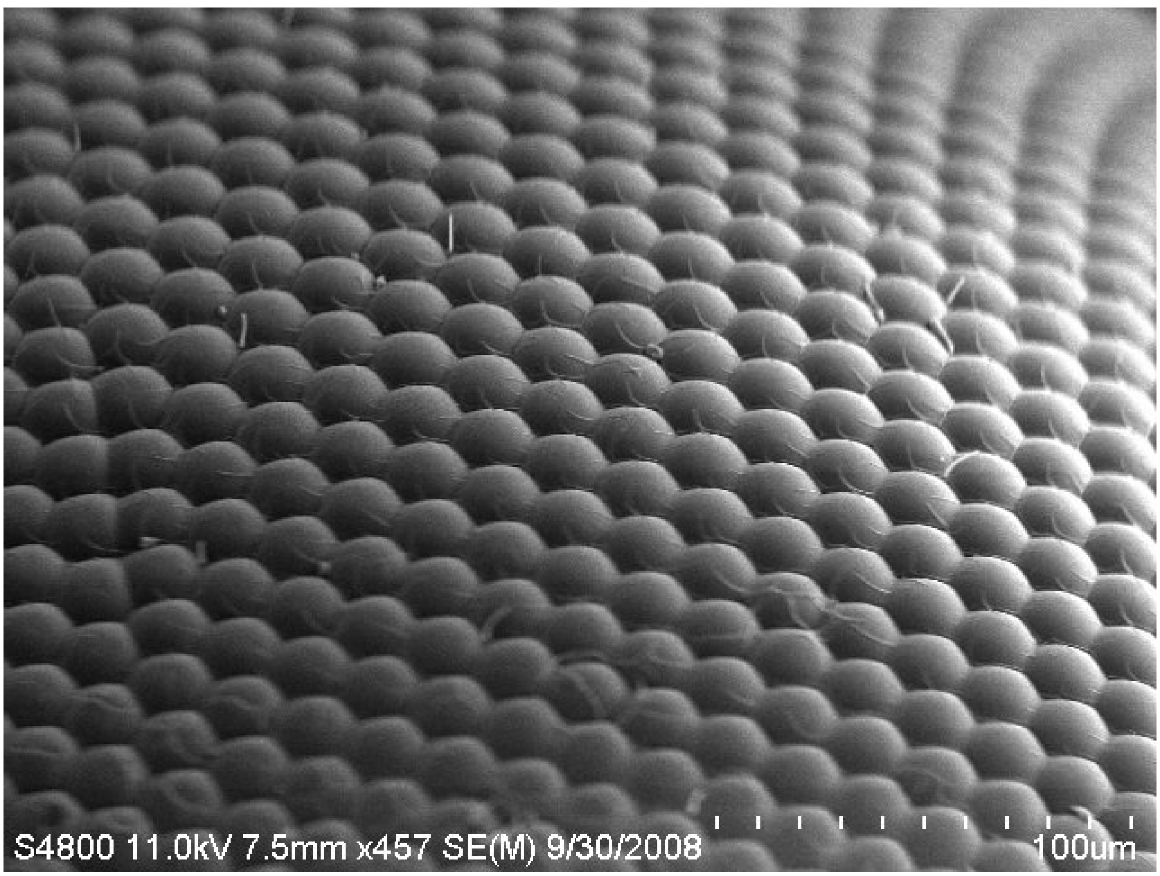
Reflector eyes

An alternative to a lens is to line the inside of the eye with " mirrors", and reflect the image to focus at a central point. The nature of these eyes means that if one were to peer into the pupil of an eye, one would see the same image that the organism would see, reflected back out.

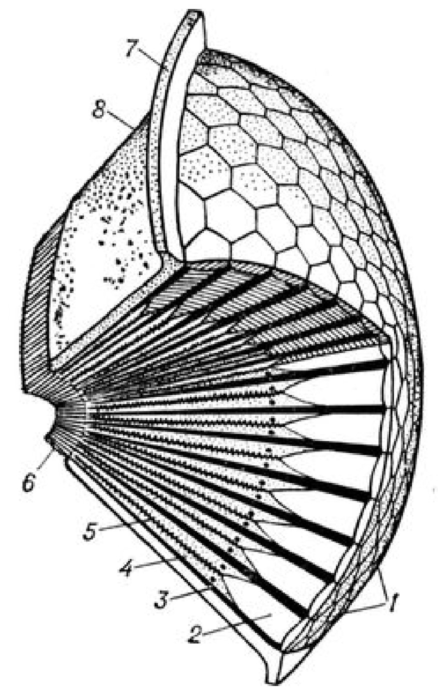
Many small organisms such as rotifers, copeopods and platyhelminths use such organs, but these are too small to produce usable images. Some larger organisms, such as scallops, also use reflector eyes. The scallop *Pecten* has up to 100 millimeter-scale reflector eyes fringing the edge of its shell. It detects moving objects as they pass successive lenses.

There is at least one vertebrate, the spookfish, whose eyes include reflective optics for focusing of light. Each of the two eyes of a spookfish collects light from both above and below; the light coming from above is focused by a lens, while that coming from below, by a curved mirror composed of many layers of small reflective plates made of guanine crystals.

Compound eyes



An image of a house fly compound eye surface by using Scanning Electron Microscope



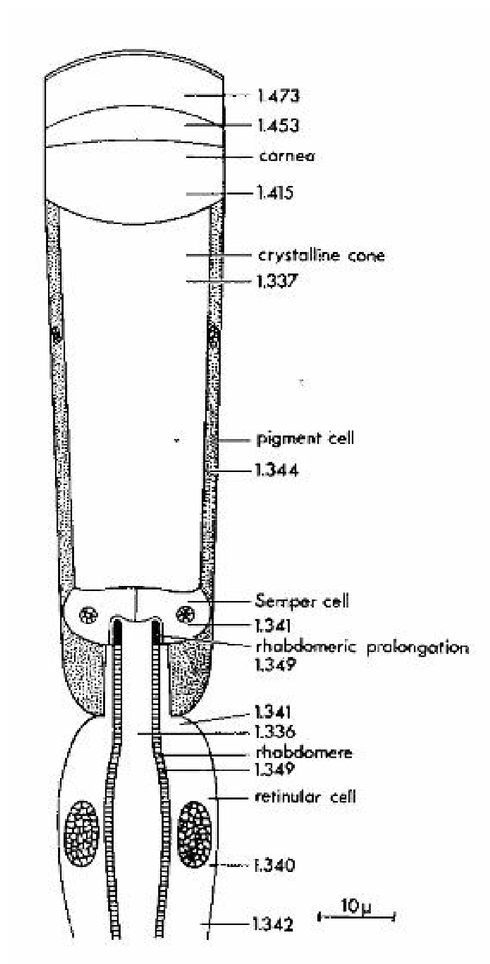
Anatomy of the compound eye of an insect

Arthropods such as this Calliphora vomitoria fly have compound eyes

A compound eye may consist of thousands of individual photoreceptor units or ommatidia (ommatidium, singular). The image perceived is a combination of inputs from the numerous ommatidia (individual "eye units"), which are located on a convex surface, thus pointing in slightly different directions. Compared with simple eyes, compound eyes possess a very large view angle, and can detect fast movement and, in some cases, the polarization of light. Because the individual lenses are so small, the effects of diffraction impose a limit on the possible resolution that can be obtained (assuming that they do not function as phased arrays). This can only be countered by increasing lens size and number. To see with a resolution comparable to our simple eyes, humans would require compound eyes which would each reach the size of their head.

Compound eyes fall into two groups: apposition eyes, which form multiple inverted images, and superposition eyes, which form a single erect image. Compound eyes are common in arthropods, and are also present in annelids and some bivalved molluscs.

Compound eyes, in arthropods at least, grow at their margins by the addition of new ommatidia.



Structure of the ommatidia of apposition compound eyes

Apposition eyes

Apposition eyes are the most common form of eye, and are presumably the ancestral form of compound eye. They are found in all arthropod groups, although they may have evolved more than once within this phylum. Some annelids and bivalves also have apposition eyes. They are also possessed by *Limulus*, the horseshoe crab, and there are suggestions that other chelicerates developed their simple eyes by reduction from a compound starting point. (Some caterpillars appear to have evolved compound eyes from simple eyes in the opposite fashion.)

Apposition eyes work by gathering a number of images, one from each eye, and combining them in the brain, with each eye typically contributing a single point of information.

The typical apposition eye has a lens focusing light from one direction on the rhabdom, while light from other directions is absorbed by the dark wall of the ommatidium. In the other kind of apposition eye, found in the Strepsiptera, lenses are not fused to one another, and each forms an entire image; these images are combined in the brain. This is called the schizochroal compound eye or the neural superposition eye. Because images are combined additively, this arrangement allows vision under lower light levels.

Superposition eyes

The second type is named the superposition eye. The superposition eye is divided into three types; the refracting, the reflecting and the parabolic superposition eye. The refracting superposition eye has a gap between the lens and the rhabdom, and no side wall. Each lens takes light at an angle to its axis and reflects it to the same angle on the other side. The result is an image at half the radius of the eye, which is where the tips of the rhabdoms are. This kind is used mostly by nocturnal insects. In the parabolic superposition compound eye type, seen in arthropods such as mayflies, the parabolic surfaces of the inside of each facet focus light from a reflector to a sensor array. Long-bodied decapod crustaceans such as shrimp, prawns, crayfish and lobsters are alone in having reflecting superposition eyes, which also have a transparent gap but use corner mirrors instead of lenses.

Parabolic superposition

This eye type functions by refracting light, then using a parabolic mirror to focus the image; it combines features of superposition and apposition eyes.

Other

Good fliers like flies or honey bees, or prey-catching insects like praying mantis or dragonflies, have specialized zones of ommatidia organized into a fovea area which gives acute vision. In the acute zone the eyes are flattened and the facets larger. The flattening allows more ommatidia to receive light from a spot and therefore higher resolution.

There are some exceptions from the types mentioned above. Some insects have a so-called single lens compound eye, a transitional type which is something between a superposition type of the multi-lens compound eye and the single lens eye found in animals with simple eyes. Then there is the mysid shrimp *Dioptromysis paucispinosa*. The shrimp has an eye of the refracting superposition type, in the rear behind this in each eye there is a single large facet that is three times in diameter the others in the eye and behind this is an enlarged crystalline cone. This projects an upright image on a specialized retina. The resulting eye is a mixture of a simple eye within a compound eye.

Another version is the pseudofaceted eye, as seen in Scutigera. This type of eye consists of a cluster of numerous ocelli on each side of the head, organized in a way that resembles a true compound eye.

The body of *Ophiocoma wendtii*, a type of brittle star, is covered with ommatidia, turning its whole skin into a compound eye. The same is true of many chitons.

Nutrients of the eye

The **ciliary body** is triangular in horizontal section and is coated by a double layer, the ciliary epithelium. The inner layer is transparent and covers the vitreous body, and is continuous from the neural tissue of the retina. The outer layer is highly pigmented, continuous with the retinal pigment epithelium, and constitutes the cells of the dilator muscle.

The **vitreous** is the transparent, colorless, gelatinous mass that fills the space between the lens of the eye and the retina lining the back of the eye. It is produced by certain retinal cells. It is of rather similar composition to the cornea, but contains very few cells (mostly phagocytes which remove unwanted cellular debris in the visual field, as well as the hyalocytes of Balazs of the surface of the vitreous, which reprocess the hyaluronic acid), no blood vessels, and 98-99% of its volume is water (as opposed to 75% in the cornea) with salts, sugars, vitrosin (a type of collagen), a network of collagen type II fibers with the mucopolysaccharide hyaluronic acid, and also a wide array of proteins in micro amounts. Amazingly, with so little solid matter, it tautly holds the eye.

Relationship to life requirements

Eyes are generally adapted to the environment and life requirements of the organism which bears them. For instance, the distribution of photoreceptors tends to match the area in which the highest acuity is required, with horizon-scanning organisms, such as those that live on the African plains, having a horizontal line of high-density ganglia, while tree-dwelling creatures which require good all-round vision tend to have a symmetrical distribution of ganglia, with acuity decreasing outwards from the centre.

Of course, for most eye types, it is impossible to diverge from a spherical form, so only the density of optical receptors can be altered. In organisms with compound eyes, it is the number of ommatidia rather than ganglia that reflects the region of highest data acquisition.[:23-4] Optical superposition eyes are constrained to a spherical shape, but other forms of compound eyes may deform to a shape where more ommatidia are aligned to, say, the horizon, without altering the size or density of individual ommatidia. Eyes of horizon-scanning organisms have stalks so they can be easily aligned to the horizon when this is inclined, for example if the animal is on a slope. An extension of this concept is that the eyes of predators typically have a zone of very acute vision at their centre, to assist in the identification of prey. In deep water organisms, it may not be the centre of the eye that is enlarged. The hyperiid amphipods are deep water animals that feed on organisms above them. Their eyes are almost divided into two, with the upper region thought to be involved in detecting the silhouettes of potential prey—or predators—against the faint light of the sky above. Accordingly, deeper water hyperiids, where the light against which the silhouettes must be compared is dimmer, have larger "upper-eyes", and may lose the lower portion of their eyes altogether. Depth perception can be enhanced by having eyes which are enlarged in one direction; distorting the eye slightly allows the distance to the object to be estimated with a high degree of accuracy.

Acuity is higher among male organisms that mate in mid-air, as they need to be able to spot and assess potential mates against a very large backdrop. On the other hand, the eyes of organisms which operate in low light levels, such as around dawn and dusk or in deep water, tend to be larger to increase the amount of light that can be captured.

It is not only the shape of the eye that may be affected by lifestyle. Eyes can be the most visible parts of organisms, and this can act as a pressure on organisms to have more transparent eyes at the cost of function.

Eyes may be mounted on stalks to provide better all-round vision, by lifting them above an organism's carapace; this also allows them to track predators or prey without moving the head.

Visual acuity

A hawk's eye

Visual acuity, or resolving power, is "the ability to distinguish fine detail" and is the property of cones. It is often measured in *cycles per degree* (CPD), which measures an angular resolution, or how much an eye can differentiate one object from another in terms of visual angles. Resolution in CPD can be measured by bar charts of different numbers of white/black stripe cycles. For example, if each pattern is 1.75 cm wide and is placed at 1 m distance from the eye, it will subtend an angle of 1 degree, so the number of white/black bar pairs on the pattern will be a measure of the cycles per degree of that pattern. The highest such number that the eye can resolve as stripes, or distinguish from a gray block, is then the measurement of visual acuity of the eye.

For a human eye with excellent acuity, the maximum theoretical resolution is 50 CPD (1.2 arcminute per line pair, or a 0.35 mm line pair, at 1 m). A rat can resolve only about 1 to 2 CPD. A horse has higher acuity through most of the visual field of its eyes than a human has, but does not match the high acuity of the human eye's central fovea region.

Spherical aberration limits the resolution of a 7 mm pupil to about 3 arcminutes per line pair. At a pupil diameter of 3 mm, the spherical aberration is greatly reduced, resulting in an improved resolution of approximately 1.7 arcminutes per line pair. A resolution of 2 arcminutes per line pair, equivalent to a 1 arcminute gap in an optotype, corresponds to 20/20 (normal vision) in humans.

Perception of colours

"Colour vision is the faculty of the organism to distinguish lights of different spectral qualities." All organisms are restricted to a small range of electromagnetic spectrum; this varies from creature to creature, but is mainly between wavelengths of 400 and 700 nm. This is a rather small section of the electromagnetic spectrum, probably reflecting the submarine evolution of the organ: water blocks out all but two small windows of the EM spectrum, and there has been no evolutionary pressure among land animals to broaden this range.

The most sensitive pigment, rhodopsin, has a peak response at 500 nm. Small changes to the genes coding for this protein can tweak the peak response by a few nm; pigments in the lens can also filter incoming light, changing the peak response. Many organisms are unable to discriminate between colours, seeing instead in shades of grey; colour vision necessitates a range of pigment cells which are primarily sensitive to smaller ranges of the spectrum. In primates, geckos, and other organisms, these take the form of cone cells, from which the more sensitive rod cells evolved. Even if organisms are physically capable of discriminating different colours, this does not necessarily mean that they can perceive the different colours; only with behavioural tests can this be deduced.

Most organisms with colour vision are able to detect ultraviolet light. This high energy light can be damaging to receptor cells. With a few exceptions (snakes, placental mammals), most organisms avoid these effects by having absorbent oil droplets around their cone cells. The alternative, developed by organisms that had lost these oil droplets in the course of evolution, is to make the lens impervious to UV light — this precludes the possibility of any UV light being detected, as it does not even reach the retina.

Rods and cones

The retina contains two major types of light-sensitive photoreceptor cells used for vision: the rods and the cones.

Rods cannot distinguish colours, but are responsible for low-light (scotopic) monochrome (black-and-white) vision; they work well in dim light as they contain a pigment, rhodopsin (visual purple), which is sensitive at low light intensity, but saturates at higher (photopic) intensities. Rods are distributed throughout the retina but there are none at the fovea and none at the blind spot. Rod density is greater in the peripheral retina than in the central retina.

Cones are responsible for colour vision. They require brighter light to function than rods require. In humans, there are three types of cones, maximally sensitive to long-wavelength, medium-wavelength, and short-wavelength light (often referred to as red, green, and blue, respectively, though the sensitivity peaks are not actually at these colours). The colour seen is the combined effect of stimuli to, and responses from, these three types of cone cells. Cones are mostly concentrated in and near the fovea. Only a few are present at the sides of the retina. Objects are seen most sharply in focus when their images fall on the fovea, as when one looks at an object directly. Cone cells and rods are connected through intermediate cells in the retina to nerve fibres of the optic nerve. When rods and cones are stimulated by light, the nerves send off impulses through these fibres to the brain.

Pigmentation

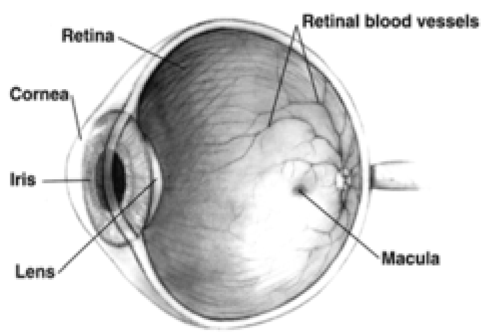
The pigment molecules used in the eye are various, but can be used to define the evolutionary distance between different groups, and can also be an aid in determining which are closely related – although problems of convergence do exist.

Opsins are the pigments involved in photoreception. Other pigments, such as melanin, are used to shield the photoreceptor cells from light leaking in from the sides. The opsin protein group evolved long before the last common ancestor of animals, and has continued to diversify since.

There are two types of opsin involved in vision; c-opsins, which are associated with ciliary-type photoreceptor cells, and r-opsins, associated with rhabdomeric photoreceptor cells. The eyes of vertebrates usually contain cilliary cells with c-opsins, and (bilaterian) invertebrates have rhabdomeric cells in the eye with r-opsins. However, some *ganglion* cells of vertebrates express r-opsins, suggesting that their ancestors used this pigment in vision, and that remnants survive in the eyes. Likewise, c-opsins have been found to be expressed in the *brain* of some invertebrates. They may have been expressed in ciliary cells of larval eyes, which were subsequently resorbed into the brain on metamorphosis to the adult form. C-opsins are also found in some derived bilaterian-invertebrate eyes, such as the pallial eyes of the bivalve molluscs; however, the lateral eyes (which were presumably the ancestral type for this group, if eyes evolved once there) always use r-opsins. Cnidaria, which are an outgroup to the taxa mentioned above, express c-opsins - but r-opsins are yet to be found in this group. Incidentally, the melanin produced in the cnidaria is produced in the same fashion as that in vertebrates, suggesting the common descent of this pigment.

Chapter 15

Retina

Retina	
	
Right human eye cross-sectional view. Courtesy NIH National Eye Institute. Many animals have eyes different from the human eye.	
Artery	central retinal artery
MeSH	*Retina*
Dorlands/Elsevier	*Retina*

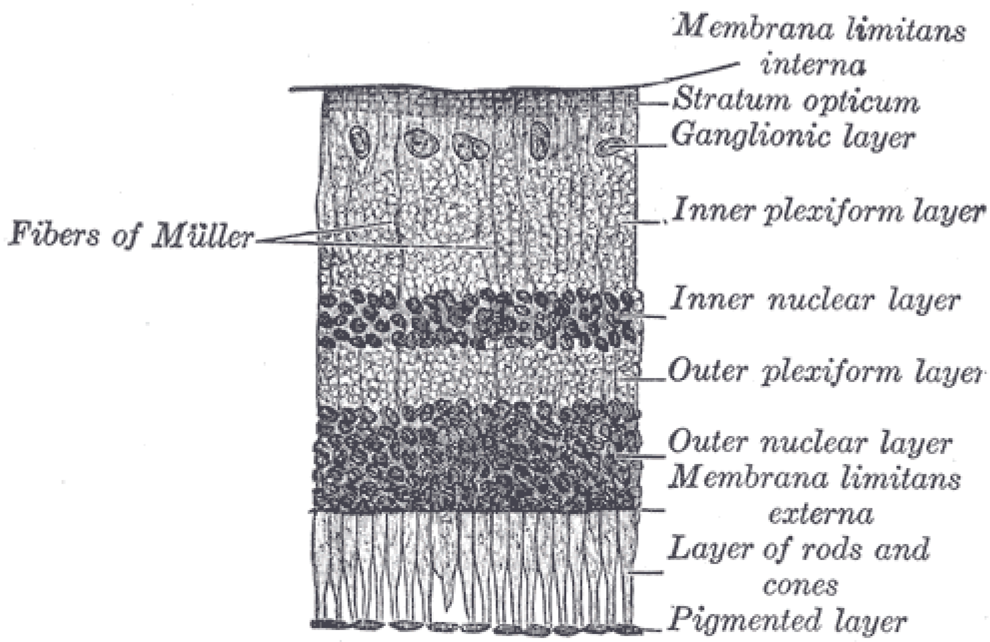
The vertebrate **retina** is a light-sensitive tissue lining the inner surface of the eye. The optics of the eye create an image of the visual world on the retina, which serves much the same function as the film in a camera. Light striking the retina initiates a cascade of chemical and electrical events that ultimately trigger nerve impulses. These are sent to various visual centers of the brain through the fibers of the optic nerve or mga vains.

In vertebrate embryonic development, the retina and the optic nerve originate as outgrowths of the developing brain, so the retina is considered part of the central nervous system (CNS). It is the only part of the CNS that can be visualized non-invasively.

The retina is a complex, layered structure with several layers of neurons interconnected by synapses. The only neurons that are directly sensitive to light are the photoreceptor cells. These are mainly of two types: the rods and cones. Rods function mainly in dim light and provide black-and-white vision, while cones support daytime vision and the perception of colour. A third, much rarer type of photoreceptor, the photosensitive ganglion cell, is important for reflexive responses to bright daylight.

Neural signals from the rods and cones undergo complex processing by other neurons of the retina. The output takes the form of action potentials in retinal ganglion cells whose axons form the optic nerve. Several important features of visual perception can be traced to the retinal encoding and processing of light.

Anatomy of vertebrate retina



Section of retina

The vertebrate retina has ten distinct layers. From closest to farthest from the vitreous body - that is, from the inner to the outer layer, they include:

1. *Inner limiting membrane* – Müller cell footplates
2. *Nerve fiber layer* – essentially the axons of the ganglion cell nuclei
3. *Ganglion cell layer* – layer that contains nuclei of ganglion cells, the axons of which become the optic nerve fibers for messages
4. *Inner plexiform layer* – contains the synapse between the bipolar cell axons and the dendrites of the ganglion and amacrine cells.
5. *Inner nuclear layer* – contains the nuclei and surrounding cell bodies (perikarya) of the bipolar cells, which correspond to heat and touch sensory skin receptors transmitting signals to the spinal cord or its continuation, the medulla.
6. *Outer plexiform layer* – projections of rods and cones ending in the rod spherule and cone pedicle, respectively. These make synapses with dendrites of bipolar In the macular region, this is known as the *Fiber layer of Henle*.
7. *Outer nuclear layer* – cell bodies of rods and cones

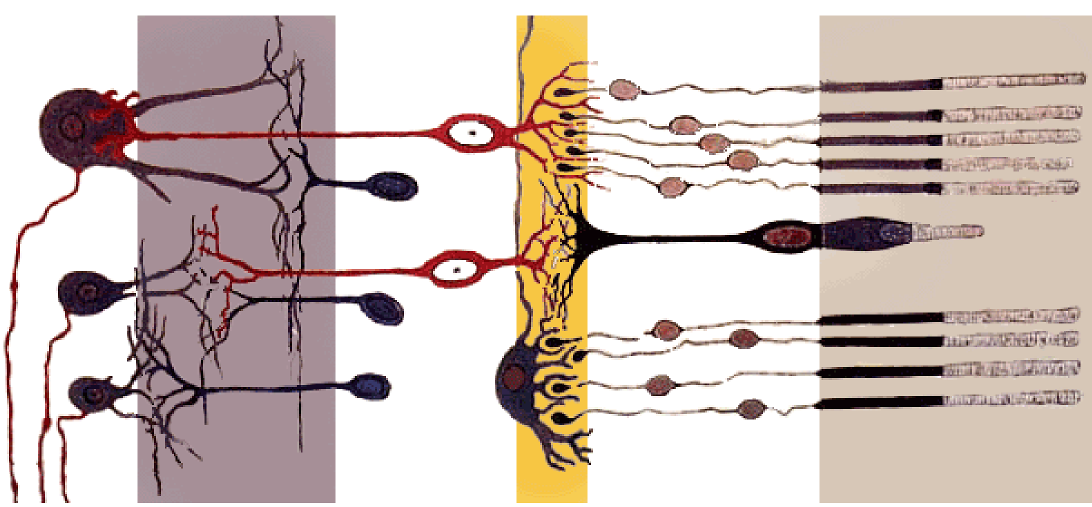
8. *External limiting membrane* – layer that separates the inner segment portions of the photoreceptors from their cell nucleus
9. *Photoreceptor layer* – rods/cones
10. *Retinal pigment epithelium*

Of these the four main layers of the ten, from outside in: pigment epithelium, the photoreceptor layer for sight, bipolar cells, and finally, the ganglion cell layer which also contains photoreceptors, the photosensitive ganglion cells.

Therefore, the optic nerve is less a nerve than a central tract, connecting the bipolars to the lateral geniculate body, a visual relay station in the diencephalon (the rear of the forebrain). Additional structures, not directly associated with vision, are found as outgrowths of the retina in some vertebrate groups. In birds, the pecten is a vascular structure of complex shape that projects from the retina into the vitreous humour; it supplies oxygen and nutrients to the eye, and may also aid in vision. Reptiles have a similar, but much simpler, structure, referred to as the *papillary cone*.

Physical structure of human retina

In adult humans the entire retina is approximately 72% of a sphere about 22 mm in diameter. The entire retina contains about 7 million cones and 75 to 150 million rods. The optic disc, a part of the retina sometimes called "the blind spot" because it lacks photoreceptors, is located at the optic papilla, a nasal zone where the optic-nerve fibers leave the eye. It appears as an oval white area of 3mm². Temporal (in the direction of the temples) to this disc is the macula. At its center is the fovea, a pit that is responsible for our sharp central vision but is actually less sensitive to light because of its lack of rods. Human and non-human primates possess one fovea as opposed to certain bird species such as hawks who actually are bifoviate and dogs and cats who possess no fovea but a central band known as the visual streak. Around the fovea extends the central retina for about 6 mm and then the peripheral retina. The edge of the retina is defined by the ora serrata. The length from one ora to the other (or macula), the most sensitive area along the horizontal meridian is about 3.2 mm.



Retina's simplified axial organization. The retina is a stack of several neuronal layers. Light is concentrated from the eye and passes across these layers (from left to right) to hit the photoreceptors (right layer). This elicits chemical transformation mediating a propagation of signal to the bipolar and horizontal cells (middle yellow layer). The signal is then propagated to the amacrine and ganglion cells. These neurons ultimately may produce action potentials on their axons. This spatiotemporal pattern of spikes determines the raw input from the eyes to the brain. (Modified from a drawing by Ramón y Cajal.)

In section the retina is no more than 0.5 mm thick. It has three layers of nerve cells and two of synapses, including the unique ribbon synapses. The optic nerve carries the ganglion cell axons to the brain and the blood vessels that open into the retina. The ganglion cells lie innermost in the retina while the photoreceptive cells lie outermost. Because of this counter-intuitive arrangement, light must first pass through and around the ganglion cells and through the thickness of the retina, (including its capillary vessels, not shown) before reaching the rods and cones. However it does not pass through the epithelium or the choroid (both of which are opaque).

The white blood cells in the capillaries in front of the photoreceptors can be perceived as tiny bright moving dots when looking into blue light. This is known as the blue field entoptic phenomenon (or Scheerer's phenomenon).

Between the ganglion cell layer and the rods and cones there are two layers of neuropils where synaptic contacts are made. The neuropil layers are the outer plexiform layer and the inner plexiform layer. In the outer the rods and cones connect to the vertically running bipolar cells, and the horizontally oriented horizontal cells connect to ganglion cells.

The central retina is cone-dominated and the peripheral retina is rod-dominated. In total there are about seven million cones and a hundred million rods. At the centre of the macula is the foveal pit where the cones are smallest and in a hexagonal mosaic, the most efficient and highest density. Below the pit the other retina layers are displaced, before building up along the foveal slope until the rim of the fovea or parafovea which is the thickest portion of the retina. The macula has a yellow pigmentation from screening pigments and is known as the macula lutea. The area directly surrounding the fovea has the highest density of rods converging on single bipolars. Since the cones have a much lesser power of merging signals, the fovea allows for the sharpest vision the eye can attain.

Though the rod and cones are a mosaic of sorts, transmission from receptors to bipolars to ganglion cells is not the case, Since there are about 150 million receptors and only 1 million optic nerve fibers, there must be convergence and thus mixing of signals. Moreover, the horizontal action of the horizontal and amacrine cells can allow one area of the retina to control another (e.g., one stimulus inhibiting another). This inhibition is key to the sum of messages sent to the higher regions of the brain. In some lower vertebrates, (e.g., the pigeon) there is a "centrifugal" control of messages, that is, one layer can control another, or higher regions of the brain can drive the retinal nerve cells, but in primates this does not occur.

Vertebrate and cephalopod retina differences

The vertebrate retina is *inverted* in the sense that the light sensing cells sit at the back side of the retina, so that light has to pass through layers of neurons and capillaries before it reaches the rods and cones. By contrast, the cephalopod retina has the photoreceptors at the front side of the retina, with processing neurons and capillaries behind them. Because of this, cephalopods do not have a blind spot.

The cephalopod retina does not originate as an outgrowth of the brain, as the vertebrate one does. It was originally argued that this difference shows that vertebrate and cephalopod eyes are not homologous but have evolved separately. The evolutionary biologist Richard Dawkins cites the imperfect structure of the human retina as confounding claims by creationists or intelligent design theorists that the human eye is so perfect it must have a designer.

In 2009 Kröger anatomically showed in Zebrafish that though the inverted arrangement is nonadaptive in that it creates avoidable scattering of light (and thus loss of light and image blur), it has space-saving advantages for small-eyed animals in which there is a minimal vitreous body, as the space between the lens and the photoreceptors' light-sensitive outer segments is completely filled with retinal cells.

Physiology

An image is produced by the patterned excitation of the cones and rods in the retina. The excitation is processed by the neuronal system and various parts of the brain working in parallel to form a representation of the external environment in the brain.

The cones respond to bright light and mediate high-resolution colour vision during daylight illumination (also called photopic vision). The rods are saturated at daylight levels and don't contribute to pattern vision. However, rods do respond to dim light and mediate lower-resolution, monochromatic vision under very low levels of illumination (called scotopic vision). The illumination in most office settings falls between these two levels and is called mesopic vision. At these light levels, both the rods and cones are actively contributing pattern information to that exiting the eye. What contribution the rod information makes to pattern vision under these circumstances is unclear.

The response of cones to various wavelengths of light is called their spectral sensitivity. In normal human vision, the spectral sensitivity of a cone falls into one of three subgroups. These are often called blue, green, and red cones but more accurately are short, medium, and long wavelength sensitive cone subgroups. It is a lack of one or more of the cone subtypes that causes individuals to have deficiencies in colour vision or various kinds of colour blindness. These individuals are not blind to objects of a particular colour but experience the inability to distinguish between two groups of colours that *can* be distinguished by people with normal vision. Humans have three different types of cones (trichromatic vision) while most other mammals lack cones with red sensitive pigment and therefore have poorer (dichromatic) colour vision. However, some animals have four spectral subgroups, e.g., the trout adds an ultraviolet subgroup to short, medium and long subgroups that are similar to humans. Some fish are sensitive to the polarization of light as well.

When light falls on a receptor it sends a proportional response synaptically to bipolar cells which in turn signal the retinal ganglion cells. The receptors are also 'cross-linked' by horizontal cells and amacrine cells, which modify the synaptic signal before the ganglion cells. Rod and cone signals are intermixed and combine, although rods are mostly active in very poorly lit conditions and saturate in broad daylight, while cones function in brighter lighting because they are not sensitive enough to work at very low light levels.

Despite the fact that all are nerve cells, only the retinal ganglion cells and few amacrine cells create action potentials. In the photoreceptors, exposure to light hyperpolarizes the membrane in a series of graded shifts. The outer cell segment contains a photopigment. Inside the cell the normal levels of cyclic guanosine monophosphate (cGMP) keep the Na+ channel open and thus in the resting state the cell is depolarised. The photon causes the retinal bound to the receptor protein to isomerise to trans-retinal. This causes receptor to activate multiple G-proteins. This in turn causes the Ga-subunit of the protein to bind and degrade cGMP inside the cell which then cannot bind to the Na+ cyclic nucleotide-gated ion channels (CNGs). Thus the cell is hyperpolarised. The amount of neurotransmitter released is reduced in bright light and increases as light levels fall. The actual photopigment is bleached away in bright light and only replaced as a chemical process, so in a transition from bright light to darkness the eye can take up to thirty minutes to reach full sensitivity.

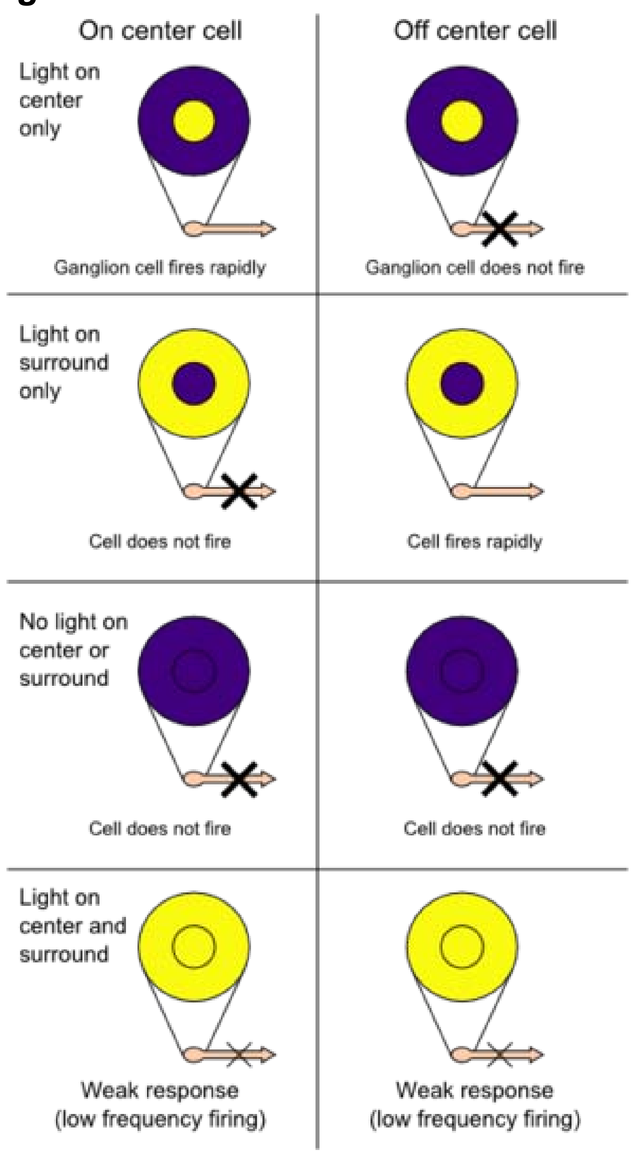
In the retinal ganglion cells there are two types of response, depending on the receptive field of the cell. The receptive fields of retinal ganglion cells comprise a central approximately circular area, where light has one effect on the firing of the cell, and an annular surround, where light has the opposite effect on the firing of the cell. In ON cells, an increment in light intensity in the centre of the receptive field causes the firing rate to increase. In OFF cells, it makes it decrease. In a linear model, this response profile is well described by a Difference of Gaussians and is the basis for edge detection algorithms. Beyond this simple difference ganglion cells are also differentiated by chromatic sensitivity and the type of spatial summation. Cells showing linear spatial summation are termed X cells (also called parvocellular, P, or midget ganglion cells), and those showing non-linear summation are Y cells (also called magnocellular, M, or parasol retinal ganglion cells), although the correspondence between X and Y cells (in the cat retina) and P and M cells (in the primate retina) is not as simple as it once seemed.

In the transfer of visual signals to the brain, the visual pathway, the retina is vertically divided in two, a temporal (nearer to the temple) half and a nasal (nearer to the nose) half.

The axons from the nasal half cross the brain at the optic chiasma to join with axons from the temporal half of the other eye before passing into the lateral geniculate body.

Although there are more than 130 million retinal receptors, there are only approximately 1.2 million fibres (axons) in the optic nerve; a large amount of pre-processing is performed within the retina. The fovea produces the most accurate information. Despite occupying about 0.01% of the visual field (less than 2° of visual angle), about 10% of axons in the optic nerve are devoted to the fovea. The resolution limit of the fovea has been determined at around 10,000 points. The information capacity is estimated at 500,000 bits per second without colour or around 600,000 bits per second including colour.

Spatial encoding



On-centers and off-centers of the retina

The retina, unlike a camera, does not simply send a picture to the brain. The retina spatially encodes (compresses) the image to fit the limited capacity of the optic nerve. Compression is necessary because there are 100 times more Photoreceptor cells than ganglion cells as mentioned above. The retina does so by "decorrelating" the incoming images in a manner to be described below. These operations are carried out by the center surround structures as implemented by the bipolar and ganglion cells.

There are two types of center surround structures in the retina—on-centers and off-centers. On-centers have a positively weighted center and a negatively weighted surround. Off-centers are just the opposite. Positive weighting is more commonly known as excitatory and negative weighting is more commonly known as inhibitory.

These center surround structures are not physical in the sense that you cannot see them by staining samples of tissue and examining the retina's anatomy. The center surround structures are logical (i.e., mathematically abstract) in the sense that they depend on the connection strengths between ganglion and bipolar cells. It is believed that the connection strengths between cells is caused by the number and types of ion channels embedded in the synapses between the ganglion and bipolar cells. Stephen Kuffler in the 1950s was the first person to begin to understand these center surround structures in the retina of cats.

The center surround structures are mathematically equivalent to the edge detection algorithms used by computer programmers to extract or enhance the edges in a digital photograph. Thus the retina performs operations on the image to enhance the edges of objects within its visual field. For example, in a picture of a dog, a cat and a car, it is the edges of these objects that contain the most information. In order for higher functions in the brain (or in a computer for that matter) to extract and classify objects such as a dog and a cat, the retina is the first step to separating out the various objects within the scene.

As an example, the following matrix is at the heart of the computer algorithm that implements edge detection. This matrix is the computer equivalent to the center surround structure. In this example, each box (element) within this matrix would be connected to one photoreceptor. The photoreceptor in the center is the current receptor being processed. The center photoreceptor is multiplied by the +1 weight factor. The surrounding photoreceptors are the "nearest neighbors" to the center and are multiplied by the -1/8 value. The sum of all nine of these elements is finally calculated. This summation is repeated for every photoreceptor in the image by shifting left to the end of a row and then down to the next line.

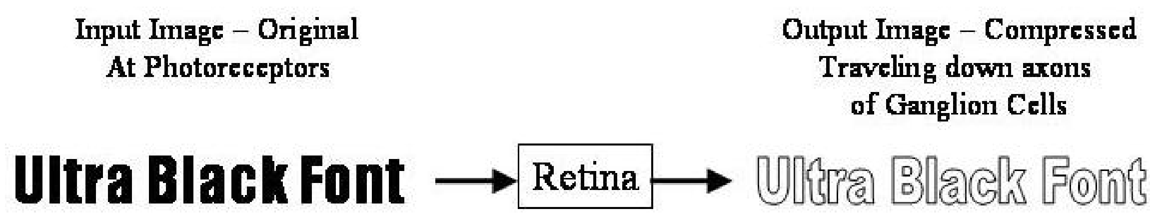
-1/8	-1/8	-1/8
-1/8	+1	-1/8
-1/8	-1/8	-1/8

The total sum of this matrix is zero if all the inputs from the nine photoreceptors are the same value. The zero result indicates the image was uniform (non-changing) within this small patch. Negative or positive sums mean something was varying (changing) within this small patch of nine photoreceptors.

The above matrix is only an approximation to what really happens inside the retina. The differences are:

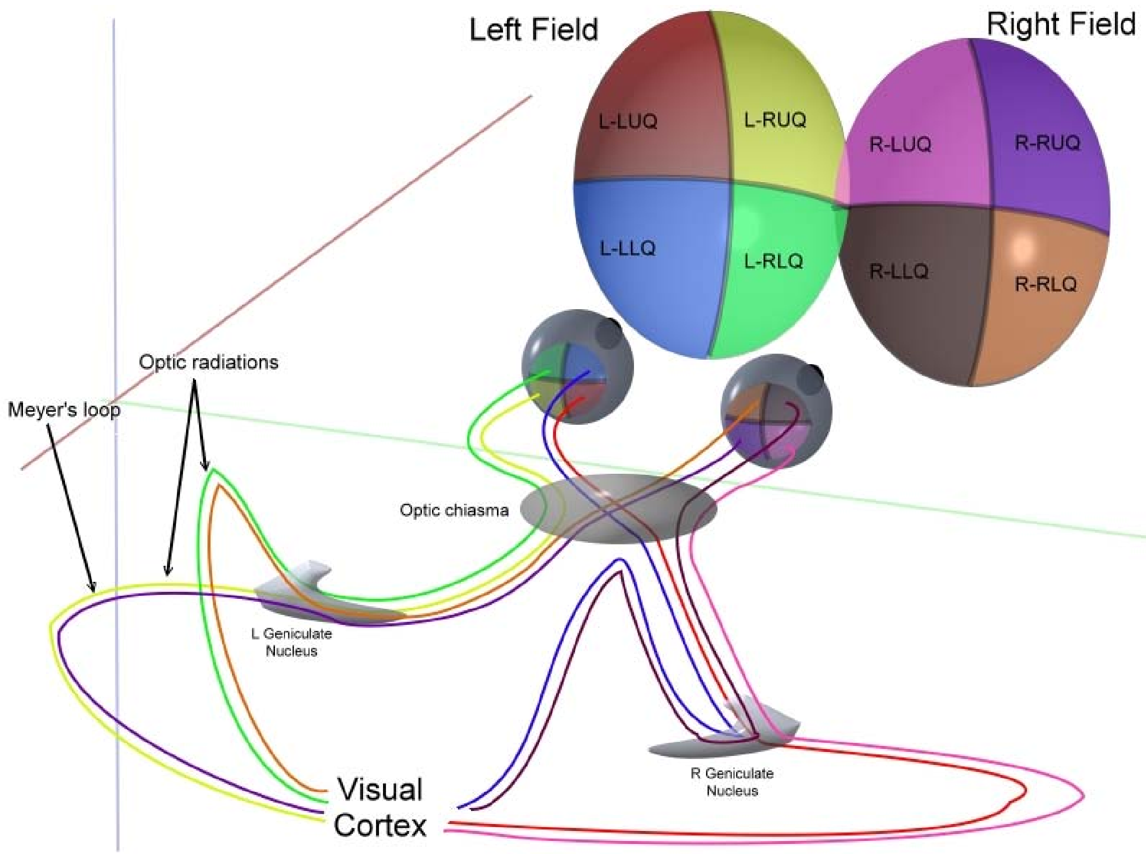
1. The above example is called "balanced". The term balanced means that the sum of the negative weights is equal to the sum of the positive weights so that they cancel out perfectly. Retinal ganglion cells are almost never perfectly balanced.
2. The table is square while the center surround structures in the retina are circular.
3. Neurons operate on spike trains traveling down nerve cell axons. Computers operate on a single Floating point number that is essentially constant from each input pixel. (The computer pixel is basically the equivalent of a biological photoreceptor.)
4. The retina performs all these calculations in parallel while the computer operates on each pixel one at a time. There are no repeated summations and shifting as there would be in a computer.
5. Finally, the horizontal and amacrine cells play a significant role in this process but that is not represented here.

Here is an example of an input image and how edge detection would modify it.



Once the image is spatially encoded by the center surround structures, the signal is sent out the optical nerve (via the axons of the ganglion cells) through the optic chiasm to the LGN (lateral geniculate nucleus). The exact function of the LGN is unknown at this time. The output of the LGN is then sent to the back of the brain. Specifically the output of the LGN "radiates" out to the V1 Primary visual cortex.

Simplified Signal Flow: Photoreceptors → Bipolar → Ganglion → Chiasm → LGN → V1 cortex



Diseases and disorders

There are many inherited and acquired diseases or disorders that may affect the retina. Some of them include:

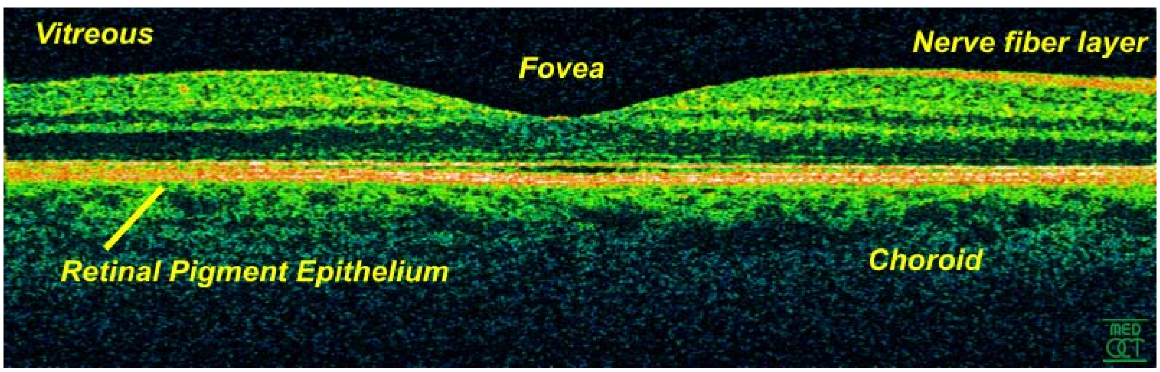
- Retinitis pigmentosa is a group of genetic diseases that affect the retina and causes the loss of night vision and peripheral vision.
- Macular degeneration describes a group of diseases characterized by loss of central vision because of death or impairment of the cells in the macula.
- Cone-rod dystrophy (CORD) describes a number of diseases where vision loss is caused by deterioration of the cones and/or rods in the retina.
- In retinal separation, the retina detaches from the back of the eyeball. Ignipuncture is an outdated treatment method. The term retinal detachment is used to describe a separation of the neurosensory retina from the retinal pigment epithelium. There are several modern treatment methods for fixing a retinal detachment: pneumatic retinopexy, scleral buckle, cryotherapy, laser photocoagulation and pars plana vitrectomy.
- Both hypertension and diabetes mellitus can cause damage to the tiny blood vessels that supply the retina, leading to hypertensive retinopathy and diabetic retinopathy.
- Retinoblastoma is a cancer of the retina.

- Retinal diseases in dogs include retinal dysplasia, progressive retinal atrophy, and sudden acquired retinal degeneration.
- *Lipemia retinalis* is a white appearance of the retina, and can occur by lipid deposition in lipoprotein lipase deficiency.

Diagnosis and treatment

A number of different instruments are available for the diagnosis of diseases and disorders affecting the retina. An ophthalmoscope is used to examine the retina. Recently, adaptive optics has been used to image individual rods and cones in the living human retina and a company based in Scotland have engineered technology that allows physicians to observe the complete retina without any discomfort to patients.

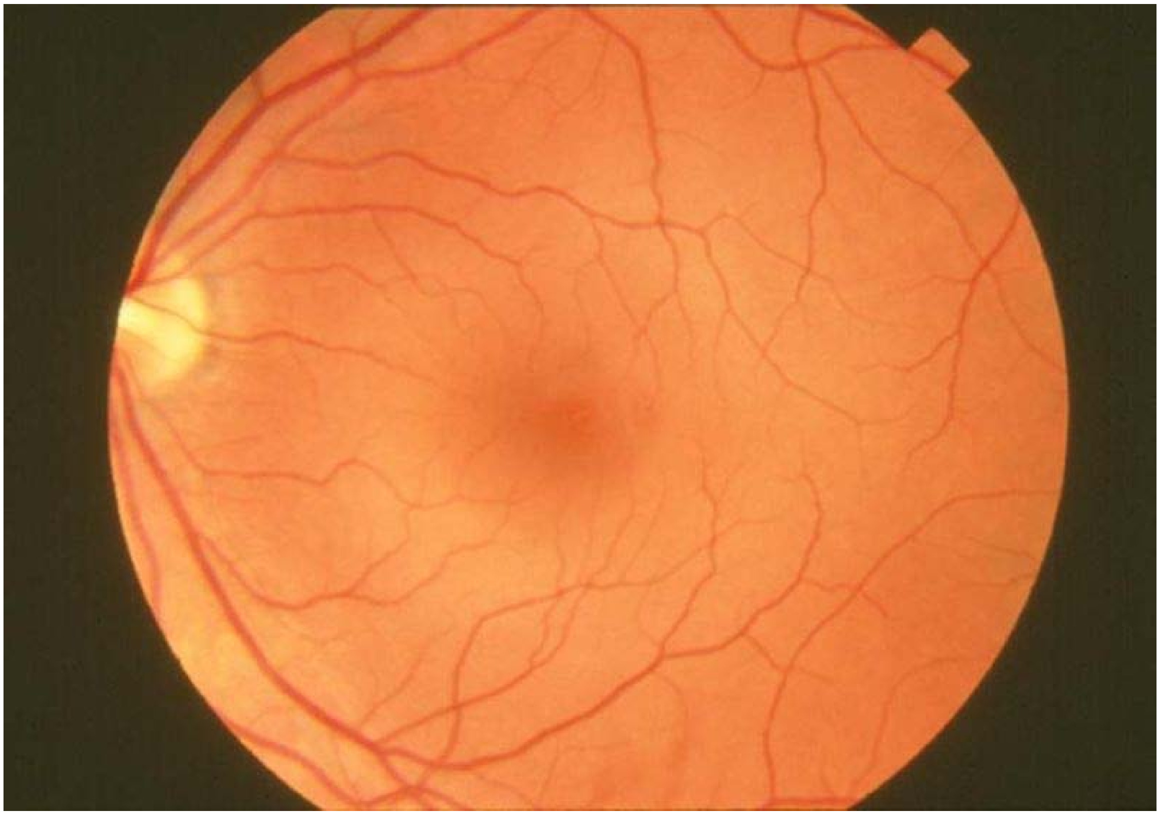
The electroretinogram is used to measure non-invasively the retina's electrical activity, which is affected by certain diseases. A relatively new technology, now becoming widely available, is optical coherence tomography (OCT). This non-invasive technique allows one to obtain a 3D volumetric or high resolution cross-sectional tomogram of the retinal fine structure with histologic-quality.



OCT scan of a retina at 800nm with an axial resolution of 3µm

Treatment depends upon the nature of the disease or disorder. Transplantation of retinas has been attempted, but without much success. At MIT, The University of Southern California, and the University of New South Wales, an "artificial retina" is under development: an implant which will bypass the photoreceptors of the retina and stimulate the attached nerve cells directly, with signals from a digital camera.

Retinal blood supply



The blood vessels in a normal human retina. The optic disk is at extreme left, and the macula lutea is near the center.

There are two circulations, both supplied by the ophthalmic artery. The uveal circulation consists of arteries entering the globe outside the optic nerve, these supply the uvea and outer and middle layers of the retina. The retinal circulation, on the other hand, supplies the inner layer of the retina and passes with the optic nerve as a branch of the ophthalmic artery called the central artery of the retina. The unique structure of the blood vessels in the retina has been used for biometric identification.

Research

George Wald, Haldan Keffer Hartline and Ragnar Granit won the 1967 Nobel Prize in Physiology or Medicine for their scientific research on the retina.

A recent University of Pennsylvania study calculated the approximate bandwidth of human retinas is 8.75 megabits per second, whereas guinea pig retinas transfer at 875 kilobits.

MacLaren & Pearson and colleagues at University College London and Moorfields Eye Hospital in London showed in 2006 that photoreceptor cells could be transplanted successfully in the mouse retina if donor cells were at a critical developmental stage.

Recently Ader and colleagues in Dublin showed using the electron microscope that transplanted photoreceptors formed synaptic connections.

Retinal gene therapy

Gene therapy holds promise as a potential avenue to cure a wide range of retinal diseases. This involves using a non-infectious virus to shuttle a gene into a part of the retina. Recombinant adeno-associated virus (rAAV) vectors possess a number of features that render them ideally suited for retinal gene therapy, including a lack of pathogenicity, minimal immunogenicity, and the ability to transduce postmitotic cells in a stable and efficient manner. rAAV vectors are increasingly utilized for their ability to mediate efficient transduction of retinal pigment epithelium (RPE), photoreceptor cells and retinal ganglion cells. Each cell type can be specifically targeted by choosing the appropriate combination of AAV serotype, promoter, and intraocular injection site.

The unique architecture of the retina and its relatively immune-privileged environment help this process. Tight junctions that form the blood retinal barrier separate the subretinal space from the blood supply, thus protecting it from microbes and most immune-mediated damage, and enhancing its potential to respond to vector-mediated therapies. The highly compartmentalized anatomy of the eye facilitates accurate delivery of therapeutic vector suspensions to specific tissues under direct visualization using microsurgical techniques. In the sheltered environment of the retina, AAV vectors are able to maintain high levels of transgene expression in the retinal pigmented epithelium (RPE), photoreceptors, or ganglion cells for long periods of time after a single treatment. In addition, the eye and the visual system can be routinely and easily monitored for visual function and retinal structural changes after injections with noninvasive advanced technology, such as visual acuities, contrast sensitivity, fundus auto-fluorescence (FAF), dark-adapted visual thresholds, vascular diameters, pupillometry, electroretinography (ERG), multifocal ERG and optical coherence tomography (OCT).

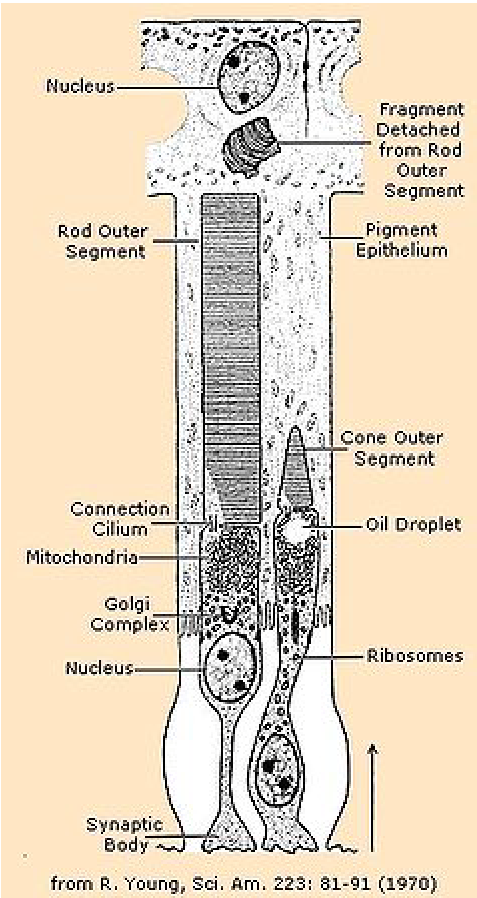
This strategy is effective against retinal diseases that have been studied including neovascular diseases that are features of age-related macular degeneration, diabetic retinopathy and retinopathy of prematurity. Since the regulation of vascularization in the mature retina involves a balance between endogenous positive growth factors, such as vascular endothelial growth factor (VEGF) and inhibitors of angiogenesis, such as pigment epithelium-derived factor (PEDF), rAAV-mediated expression of PEDF, angiostatin, and the soluble VEGF receptor sFlt-1, which are all antiangiogenic proteins, have been shown to reduce aberrant vessel formation in animal models. Since specific gene therapies cannot readily be used to treat a significant fraction of patients with retinal dystrophy, there is a major interest in developing a more generally applicable survival factor therapy. Neurotrophic factors have the ability to modulate neuronal growth during development to maintain existing cells and to allow recovery of injured neuronal populations in the eye. AAV encoding neurotrophic factors such as fibroblast growth factor (FGF) family members and GDNF either protected photoreceptors from apoptosis or slowed down cell death.

However, treatment of inherited retinal degenerative diseases such as retinitis pigmentosa and Leber congenital amaurosis (LCA) via gene replacement therapy constitutes the most straightforward and therefore the most promising approach for treating the autosomal recessive retinal disease. Leber Congenital Amaurosis (LCA2) is a defect of the *RPE65* gene, which is responsible for the synthesis of 11-cis retinal, an important molecule in the visual phototransduction, and gene replacement therapy studies utilizing *rpe65*-encoding AAV have yielded hopeful results in animal models. Based on several encouraging reports from animal models, at least three clinical trials are currently underway for the treatment of LCA using modified AAV vectors carrying the RPE65 cDNA and have reported positive preliminary results.

Chapter 16

Photoreceptor Cell

Neuron: Photoreceptor Cell



Functional parts of the rods and cones which are two of the three types of photosensitive cells in the retina

NeuroLex ID *sao1233810115*

A **photoreceptor cell** is a specialized type of neuron found in the eye's retina that is capable of phototransduction. The great biological importance of photoreceptors is that they convert light (electromagnetic radiation) into signals that can stimulate biological processes. More specifically, photoreceptor proteins in the cell absorb photons, triggering a change in the cell's membrane potential.

The two classic photoreceptor cells are rods and cones, each contributing information used by the visual system to form a representation of the visual world, sight. The rods are narrower than the cones and distributed differently across the retina, but the chemical process in each which supports phototransduction is similar. A third class of photoreceptor cells was discovered during the 1990s: the photosensitive ganglion cells. These cells do not contribute to sight directly, but are thought to support circadian rhythms and pupillary reflex.

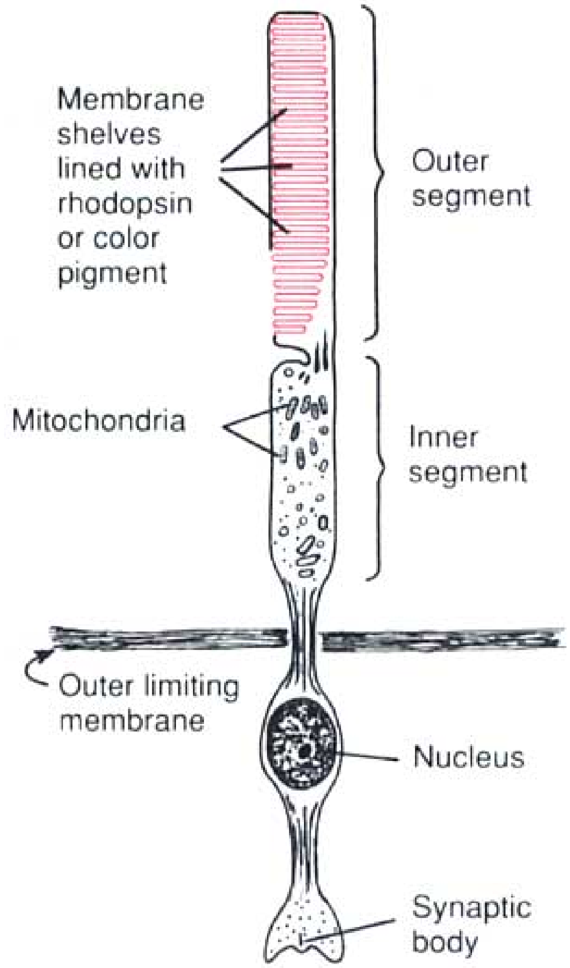
There are major functional differences between the rods and cones. Rods are extremely sensitive, and can be triggered by a very small number of photons. At very low light levels, visual experience is calculated solely from the rod signal. This explains why colors cannot be seen at low light levels: only one type of photoreceptor cell is active.

Cones require significantly brighter light (i.e. a larger numbers of photons) in order to produce a signal. In humans there are three different types of cone cell, distinguished by their pattern of response to different wavelengths of light. Color experience is calculated from these three distinct signals, perhaps via an opponent process. The three types of cone cell respond (roughly) to light of short, medium, and long wavelengths. Note that due to the principle of univariance the firing of the cell depends only upon the number of photons absorbed. The different responses of the three types of cone cells are determined by the likelihoods that their respective photoreceptor proteins will absorb photons of different wavelengths. So, for example, an L cone cell contains a photoreceptor protein which more readily absorbs long wavelengths of light (i.e. more "red"). Light of a shorter wavelength can also produce the same response, but it must be much brighter to do so.

The human retina contains about 120 million rod cells and 5 million cone cells. The number and ratio of rods to cones varies among species, dependent on whether an animal is primarily diurnal or nocturnal. Certain owls have a tremendous number of rods in their retinas — the eyes of the tawny owl are approximately 100 times more sensitive at night than those of humans. There are about 1.3 million ganglion cells in the human visual system; 1 to 2% of them are photosensitive.

Described here are vertebrate photoreceptors. Invertebrate photoreceptors in organisms such as insects and molluscs are different in both their morphological organization and their underlying biochemical pathways.

Histology



Anatomy of a Rod Cell

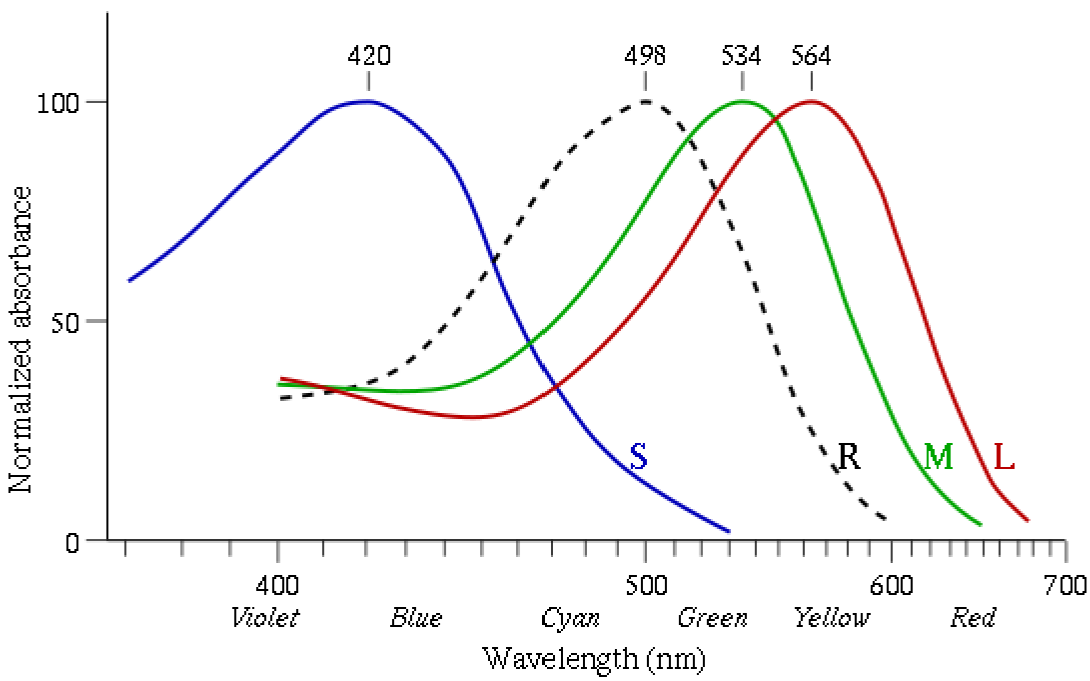
Rod and cone photoreceptors are found on the outermost layer of the retina; they both have the same basic structure. Closest to the visual field (and farthest from the brain) is the axon terminal, which releases a neurotransmitter called glutamate to bipolar cells. Farther back is the cell body, which contains the cell's organelles. Farther back still is the inner segment, a specialized part of the cell full of mitochondria. The chief function of the inner segment is to provide ATP (energy) for the sodium-potassium pump. Finally, closest to the brain (and farthest from the field of view) is the outer segment, the part of the photoreceptor that absorbs light. Outer segments are actually modified cilia that contain disks filled with opsin, the molecule that absorbs photons, as well as voltage-gated sodium channels.

The membranous photoreceptor protein *opsin* contains a pigment molecule called *retinal*. In rod cells, these together are called rhodopsin. In cone cells there are different types of opsins that combine with retinal to form pigments called photopsins. Three different classes of photopsins in the cones react to different ranges of light frequency, a differentiation which allows the visual system to calculate color. The function of the photoreceptor cell is to convert the light energy of the photon into a form of energy communicable to the nervous system and readily usable to the organism: this conversion is called signal transduction.

The opsin found in the photosensitive ganglion cells of the retina that are involved in various reflexive responses of the brain and body to the presence of (day)light, such as the regulation of circadian rhythms, pupillary reflex and other non-visual responses to light, is called melanopsin. Atypical in vertebrates, melanopsin functionally resembles invertebrate opsins. In structure, it is an opsin, a retinylidene protein variety of G-protein-coupled receptor.

When light activates the melanopsin signaling system, the melanopsin-containing ganglion cells discharge nerve impulses which are conducted through their axons to specific brain targets. These targets include the olivary pretectal nucleus (a center responsible for controlling the pupil of the eye), the LGN, and, through the retinohypothalamic tract (RHT), the suprachiasmatic nucleus of the hypothalamus (the master pacemaker of circadian rhythms). Melanopsin-containing ganglion cells are thought to influence these targets by releasing from their axon terminals the neurotransmitters glutamate and pituitary adenylate cyclase activating polypeptide (PACAP).

Humans



Normalized human photoreceptor absorbances for different wavelengths of light

The human retina has approximately 5 million cones and 120 million rods. Signals from the rods and cones converge on ganglion and bipolar cells for preprocessing before they are sent to the lateral geniculate nucleus. At the "center" of the retina (the point directly behind the lens) is the fovea, which contains only cone photoreceptor cells; this is the region capable of producing the highest visual acuity. Across the rest of the retina, rods and cones are intermingled. No photoreceptors are found at the blind spot, the area where ganglion cell fibers are collected into the optic nerve and leave the eye.

The photoreceptor proteins in the three types of cones differ in their sensitivity to photons of different wavelengths. Since cones respond to both the wavelength and intensity of light, the cone's sensitivity to wavelength is measured in terms of its relative rate of response if the intensity of a stimulus is held fixed, while the wavelength is varied. From this, in turn, is inferred the absorbance. The graph normalizes the degree of absorbance on a hundred point scale. For example, the S cone's relative response peaks around 420 nm (nanometers, a measure of wavelength). This tells us that an S cone is more likely to absorb a photon at 420 nm than at any other wavelength. If light of a different wavelength to which it is less sensitive, say 480 nm, is increased in brightness appropriately, however, it will produce exactly the same response in the S cone. So, the colors of the curves are misleading. Cones cannot detect color by themselves; rather, color vision requires comparison of the signal across different cone types.

Phototransduction

Phototransduction is the complex process whereby the energy of a photon is used to change the inherent membrane potential of the photoreceptor. This change thereby signals to the nervous system that light is in the visual field.

Activation of rods and cones is actually hyperpolarization; when they are not being stimulated, they depolarize and release glutamate continuously. In the dark, cells have a relatively high concentration of cyclic guanosine 3'-5' monophosphate (cGMP), which opens ion channels (largely sodium channels, though calcium can enter through these channels as well). The positive charges of the ions that enter the cell down its electrochemical gradient change the cell's membrane potential, cause depolarization, and lead to the release of the neurotransmitter glutamate. Glutamate can depolarize some neurons and hyperpolarize others.

When light hits a photoreceptive pigment within the photoreceptor cell, the pigment changes shape. The pigment, called iodopsin or rhodopsin, consists of large proteins called opsin (situated in the plasma membrane), attached to a covalently-bound prosthetic group: an organic molecule called retinal (a derivative of vitamin A). The retinal exists in the 11-cis-retinal form when in the dark, and stimulation by light causes its structure to change to all-trans-retinal. This structural change causes it to activate a regulatory protein called transducin, which leads to the activation of cGMP phosphodiesterase, which breaks cGMP down into 5'-GMP. Reduction in cGMP allows the ion channels to close, preventing the influx of positive ions, hyperpolarizing the cell, and stopping the release of neurotransmitters. The entire process by which light initiates a sensory response is called visual phototransduction.

Dark current

Unstimulated (in the dark), cyclic-nucleotide gated channels in the outer segment are open because cyclic GMP (cGMP) is bound to them. Hence, positively charged ions (namely sodium ions) enter the photoreceptor, depolarizing it to about −40 mV (resting potential in other nerve cells is usually −65 mV). This depolarizing current is often known as dark current.

Signal transduction pathway

The signal transduction pathway is the mechanism by which the energy of a photon signals a mechanism in the cell that leads to its electrical polarization. This polarization ultimately leads to either the transmittance or inhibition of a neural signal that will be fed to the brain via the optic nerve. The steps, or signal transduction pathway, in the vertebrate eye's rod and cone photoreceptors are then:

1. The rhodopsin or iodopsin in the outer segment absorbs a photon, changing the configuration of a retinal Schiff base cofactor inside the protein from the cis-form to the trans-form, causing the retinal to change shape.
2. This results in a series of unstable intermediates, the last of which binds stronger to the G protein in the membrane and activates transducin, a protein inside the cell. This is the first amplification step – each photoactivated rhodopsin triggers activation of about 100 transducins. (The shape change in the opsin activates a G protein called transducin.)
3. Each transducin then activates the enzyme cGMP-specific phosphodiesterase (PDE).
4. PDE then catalyzes the hydrolysis of cGMP. This is the second amplification step, where a single PDE hydrolyses about 1000 cGMP molecules. (The enzyme hydrolyzes the second messenger cGMP to GMP)
5. With the intracellular concentration of cGMP reduced, the net result is closing of cyclic nucleotide-gated ion channels in the photoreceptor membrane because cGMP was keeping the channels open. (Because cGMP acts to keep Na^+ ion channels open, the conversion of cGMP to GMP closes the channels.)
6. As a result, sodium ions can no longer enter the cell, and the photoreceptor hyperpolarizes (its charge inside the membrane becomes more negative). (The closing of Na^+ channels hyperpolarizes the cell.)
7. This change in the cell's membrane potential causes voltage-gated calcium channels to close. This leads to a decrease in the influx of calcium ions into the cell and thus the intracellular calcium ion concentration falls.
8. The lack of calcium means that less glutamate is released to the bipolar cell than before (see below). (The decreased calcium level slows the release of the neurotransmitter glutamate, which can either excite or inhibit the postsynaptic bipolar cells.)

9. Reduction in the release of glutamate means one population of bipolar cells will be depolarized and a separate population of bipolar cells will be hyperpolarized, depending on the nature of receptors (ionotropic or metabotropic) in the postsynaptic terminal.

Thus, a rod or cone photoreceptor actually releases less neurotransmitter when stimulated by light.

ATP provided by the inner segment powers the sodium-potassium pump. This pump is necessary to reset the initial state of the outer segment by taking the sodium ions that are entering the cell and pumping them back out.

Although photoreceptors are neurons, they do not conduct action potentials with the exception of the photosensitive ganglion cell -which are mainly involved in the regulation of circadian rhythms, melatonin, and control of pupil dilation.

Advantages

Phototransduction in rods and cones is unique in that the stimulus (in this case, light) actually reduces the cell's response or firing rate, which is unusual for a sensory system where the stimulus usually increases the cell's response or firing rate. However, this system offers several key advantages.

First, the classic (rod or cone) photoreceptor is depolarized in the dark, which means many sodium ions are flowing into the cell. Thus, the random opening or closing of sodium channels will not affect the membrane potential of the cell; only the closing of a large number of channels, through absorption of a photon, will affect it and signal that light is in the visual field. Hence, the system is noiseless.

Second, there is a lot of amplification in two stages of classic phototransduction: one pigment will activate many molecules of transducin, and one PDE will cleave many cGMPs. This amplification means that even the absorption of one photon will affect membrane potential and signal to the brain that light is in the visual field. This is the main feature which differentiates rod photoreceptors from cone photoreceptors. Rods are extremely sensitive and have the capacity of registering a single photon of light unlike cones. On the other hand, cones are known to have very fast kinetics in terms of rate of amplification of phototransduction unlike rods.

Difference between rods and cones

Comparison of human rod and cone cells, from Eric Kandel et al. in *Principles of Neural Science*.

Rods	Cones
Used for scotopic vision	Used for photopic vision
Very light sensitive; sensitive to scattered light	Not very light sensitive; sensitive to only direct light
Loss causes night blindness	Loss causes legal blindness
Low visual acuity	High visual acuity; better spatial resolution
Not present in fovea	Concentrated in fovea
Slow response to light, stimuli added over time	Fast response to light, can perceive more rapid changes in stimuli
Have more pigment than cones, so can detect lower light levels	Have less pigment than rods, require more light to detect images
Stacks of membrane-enclosed disks are unattached to cell membrane directly	Disks are attached to outer membrane
20 times more rods than cones in the retina	
One type of photosensitive pigment	Three types of photosensitive pigment in humans
Confer achromatic vision	Confer color vision

Function

Photoreceptors do not signal color; they only signal the presence of light in the visual field.

A given photoreceptor responds to both the wavelength and intensity of a light source. For example, red light at a certain intensity can produce the same exact response in a photoreceptor as green light of a different intensity. Therefore, the response of a single photoreceptor is ambiguous when it comes to color.

To determine color, the visual system compares responses across a population of photoreceptors (specifically, the three different cones with differing absorption spectra). To determine intensity, the visual system computes how many photoreceptors are responding. This is the mechanism that allows trichromatic color vision in humans and some other animals.

Signaling

The rod and cone photoreceptors signal their absorption of photons via a decrease in the release of the neurotransmitter glutamate to bipolar cells at its axon terminal. Since the photoreceptor is depolarized in the dark, a high amount of glutamate is being released to bipolar cells in the dark. Absorption of a photon will hyperpolarize the photoreceptor and therefore result in the release of *less* glutamate at the presynaptic terminal to the bipolar cell.

Every rod or cone photoreceptor releases the same neurotransmitter, glutamate. However, the effect of glutamate differs in the bipolar cells, depending upon the type of receptor imbedded in that cell's membrane. When glutamate binds to an ionotropic receptor, the bipolar cell will depolarize (and therefore will hyperpolarize with light as less glutamate is released). On the other hand, binding of glutamate to a metabotropic receptor results in a hyperpolarization, so this bipolar cell will depolarize to light as less glutamate is released.

In essence, this property allows for one population of bipolar cells that gets excited by light and another population that gets inhibited by it, even though all photoreceptors show the same response to light. This complexity becomes both important and necessary for detecting color, contrast, edges, etc.

Further complexity arises from the various interconnections among bipolar cells, horizontal cells, and amacrine cells in the retina. The final result is differing populations of ganglion cells in the retina, a sub-population of which is also intrinsically photosensitive, using the photopigment melanopsin.

Ganglion cell (non-rod non-cone) photoreceptors

A non-rod non-cone photoreceptor in the eyes of mice, which was shown to mediate circadian rhythms, was discovered in 1991 by Foster *et al.* These neuronal cells, called intrinsically photosensitive retinal ganglion cells (ipRGC), are a small subset (~1–3%) of the retinal ganglion cells located in the inner retina, that is, in front of the rods and cones located in the outer retina. These light sensitive neurons contain a photopigment, melanopsin, which has an absorption peak of the light at a different wavelength (~480 nm) than rods and cones. Beside circadian / behavioral functions, ipRGCs have a role in initiating the pupillary light reflex.

Dennis Dacey with colleagues showed in a species of Old World monkey that giant ganglion cells expressing melanopsin projected to the lateral geniculate nucleus (LGN). Previously only projections to the midbrain (pre-tectal nucleus) and hypothalamus (suprachiasmatic nucleus) had been shown. However a visual role for the receptor was still unsuspected and unproven.

In 2007, Farhan H. Zaidi and colleagues published pioneering work using rodless coneless humans. *Current Biology* subsequently announced in their 2008 editorial, commentary and despatches to scientists and ophthalmologists, that the non-rod non-cone photoreceptor had been conclusively discovered in humans using landmark experiments on rodless coneless humans by Zaidi and colleagues As had been found in other mammals, the identity of the non-rod non-cone photoreceptor in humans was found to be a ganglion cell in the inner retina. The workers had tracked down patients with rare diseases wiping out classic rod and cone photoreceptor function but preserving ganglion cell function. Despite having no rods or cones the patients continued to exhibit circadian photoentrainment, circadian behavioural patterns, melanopsin suppression, and pupil reactions, with peak spectral sensitivities to environmental and experimental light matching that for the melanopsin photopigment. Their brains could also associate vision with light of this frequency.

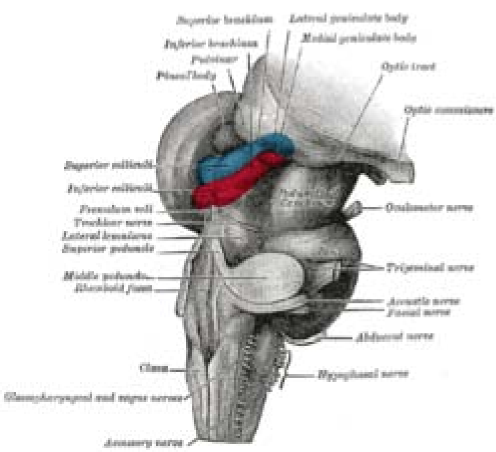
In humans the retinal ganglion cell photoreceptor contributes to conscious sight as well as to non-image-forming functions like circadian rhythms, behaviour and pupil reactions. Since these cells respond mostly to blue light, it has been suggested that they have a role in mesopic vision. Zaidi and colleagues' work with rodless coneless human subjects hence also opened the door into image-forming (visual) roles for the ganglion cell photoreceptor. It was discovered that there are parallel pathways for vision – one classic rod and cone-based arising from the outer retina, the other a rudimentary visual brightness detector arising from the inner retina and which seems to be activated by light before the other. Classic photoreceptors also feed into the novel photoreceptor system, and colour constancy may be an important role as suggested by Foster. The receptor could be instrumental in understanding many diseases including major causes of blindness worldwide like glaucoma, a disease which affects ganglion cells, and the study of the receptor offered potential as a new avenue to explore in trying to find treatments for blindness. It is in these discoveries of the novel photoreceptor in humans and in the receptors role in vision, rather than its non-image-forming functions, where the receptor may have the greatest impact on society as a whole, though the impact of disturbed circadian rhythms is another area of relevance to clinical medicine.

Most work suggests that the peak spectral sensitivity of the receptor is between 460 and 482 nm. Steven Lockley et al. in 2003 showed that 460 nm wavelengths of light suppress melatonin twice as much as longer 555 nm light. However, in more recent work by Farhan Zaidi et al., using rodless coneless humans, it was found that what consciously led to light perception was a very intense 481 nm stimulus; this means that the receptor in visual terms enables some rudimentary vision maximally for blue light.

Chapter 17

Lateral Geniculate Nucleus

Brain: Lateral geniculate nucleus



Hind- and mid-brains; postero-lateral view. (Lateral geniculate body visible near top.)

Latin	*nucleus geniculatus lateralis*
Part of	Thalamus
System	Visual
Artery	Anterior choroidal and Posterior cerebral
Vein	Terminal vein
NeuroNames	*hier-335*
NeuroLex ID	*birnlex_1662*

The **lateral geniculate nucleus** (**LGN**) is the primary relay center for visual information received from the retina of the eye. The LGN is found inside the thalamus of the brain.

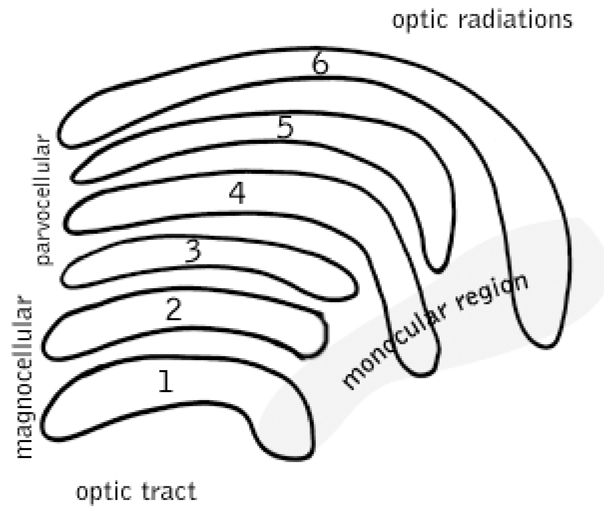
The LGN receives information directly from the ascending retinal ganglion cells via the optic tract and from the reticular activating system. Neurons of the LGN send their axons through the optic radiation, a pathway directly to the primary visual cortex. In addition, the LGN receives many strong feedback connections from the primary visual cortex. In mammals and humans the two strongest pathways linking the eye to the brain are those projecting to the LGNd (dorsal part of the LGN in the thalamus), and to the Superior Colliculus (SC)

Structure

Both the left and right hemisphere of the brain have a lateral geniculate nucleus, named so for its resemblance to a bent knee (*genu* is Latin for "knee"). In many primates, including humans and macaques, it has layers of cell bodies with layers of neuropil in between, in an arrangement something like a club sandwich or layer cake, with cell bodies of LGN neurons as the "cake" and neuropil as the "icing". In humans and macaques the LGN is normally described as having six distinctive layers. The inner two layers, 1 and 2, are called the magnocellular layers, while the outer four layers, 3, 4, 5, and 6, are called parvocellular layers. An additional set of neurons, known as the koniocellular sublayers, are found ventral to each of the magnocellular and parvocellular layers. It must be noted, this layering is variable between primate species, and extra leafleting is variable within species.

M, P, K cells

Type	Size*	Source / Type of Information	Location	Response	Number
M: Magnocellular cells	Large	Rods; necessary for the perception of **movement**, depth, and small differences in brightness	Layers 1 and 2	rapid and transient	95% (120 Mio)
P: Parvocellular cells (or "parvicellular")	Small	Cones; long- and medium-wavelength ("red" and "green" cones); necessary for the perception of **color** and form (fine details).	Layers 3, 4, 5 and 6	slow and sustained	5% (6 Mio)
K: Koniocellular cells (or "interlaminar")	Very small cell bodies	Short-wavelength "blue" cones.	Between each of the M and P layers		



Schematic diagram of the primate LGN. Layers 1 and 2 are more ventrally located, and are next to the incoming optic tract fibers.

- Size relates to cell body, dendritic tree and receptive field

The magnocellular, parvocellular, and koniocellular layers of the LGN correspond with the similarly-named types of ganglion cells.

Koniocellular cells are functionally and neurochemically distinct from M and P cells and provide a third channel to the visual cortex. They project their axons between the layers of the lateral geniculate nucleus where M and P cells project. Their role in visual perception is presently unclear; however, the koniocellular system has been linked with the integration of somatosensory system-proprioceptive information with visual perception, and it may also be involved in color perception.

The parvo- and magnocellular fibers were previously thought to dominate the Ungerleider-Mishkin ventral stream and dorsal stream, respectively. However, new evidence has accumulated showing that the two streams appear to feed on a more even mixture of different types of nerve fibers.

The other major retino-cortical visual pathway is the retinotectal pathway, routing primarily through the superior colliculus and thalamic pulvinar nucleus onto posterior parietal cortex and visual area MT.

Ipsilateral and contralateral layers

Both the LGN in the right hemisphere and the LGN in the left hemisphere receive input from each eye. However, each LGN only receives information from one half of the visual field. This occurs due to axons of the ganglion cells from the inner halves of the retina (the nasal sides) decussating (crossing to the other side of the brain) through the optic chiasm (*khiasma* means "cross"). The axons of the ganglion cells from the outer half of the retina (the temporal sides) remain on the same side of the brain. Therefore, the right hemisphere receives visual information from the left visual field, and the left hemisphere receives visual information from the right visual field. Within one LGN, the visual information is divided among the various layers as follows:

- the eye on the same side (the *ipsilateral* eye) sends information to layers 2, 3 and 5
- the eye on the opposite side (the *contralateral* eye) sends information to layers 1, 4 and 6.

A simple mnemonic for remembering this is "See I? I see, I see," with "see" representing the C in "contralateral," and "I" representing the I in "ipsilateral."

Another way of remembering this is 2+3=5, which is correct, so ipsilateral side, and 1+4 doesn't equal 6, so contralateral.

This description applies to the LGN of many primates, but not all. The sequence of layers receiving information from the ipsilateral and contralateral (opposite side of the head) eyes is different in the tarsier. Some neuroscientists suggested that "this apparent difference distinguishes tarsiers from all other primates, reinforcing the view that they arose in an early, independent line of primate evolution".

In visual perception, the right eye gets information from the right side of the world (the right visual field), as well as the left side of the world (the left visual field). You can confirm this by covering your left eye: the right eye still sees to your left and right, although on the left side your field of view is partially blocked by your nose.

In the LGN, the corresponding information from the right and left eyes is "stacked" so that a toothpick driven through the club sandwich of layers 1 through 6 would hit the same point in visual space six different times.

LGN inputs

The LGN receives input from many sources, including the cortex and then sends its output to the cortex.

At least in some species, the LGN also receives some inputs from the optic tectum (also known as the superior colliculus).

LGN output

Information leaving the LGN travels out on the optic radiations, which form part of the retrolenticular limb of the internal capsule.

The axons that leave the LGN go to V1 visual cortex. Both the magnocellular layers 1-2 and the parvocellular layers 3-6 send their axons to layer 4 in V1. Within layer 4 of V1, layer 4cβ receives parvocellular input, and layer 4cα receives magnocellular input. However, the koniocellular layers (in between layers 1-6) send their axons to layers 4a in V1. Axons from layer 6 of visual cortex send information back to the LGN.

Studies involving blindsight have suggested that projections from the LGN not only travel to the primary visual cortex but also to higher cortical areas V2 and V3. Patients with blindsight are phenomenally blind in certain areas of the visual field corresponding to a contralateral lesion in primary visual cortex; however, these patients are able to perform certain motor tasks accurately in their blind field, such as grasping. This suggests that neurons travel from the LGN to both the visual cortex and higher cortex regions.

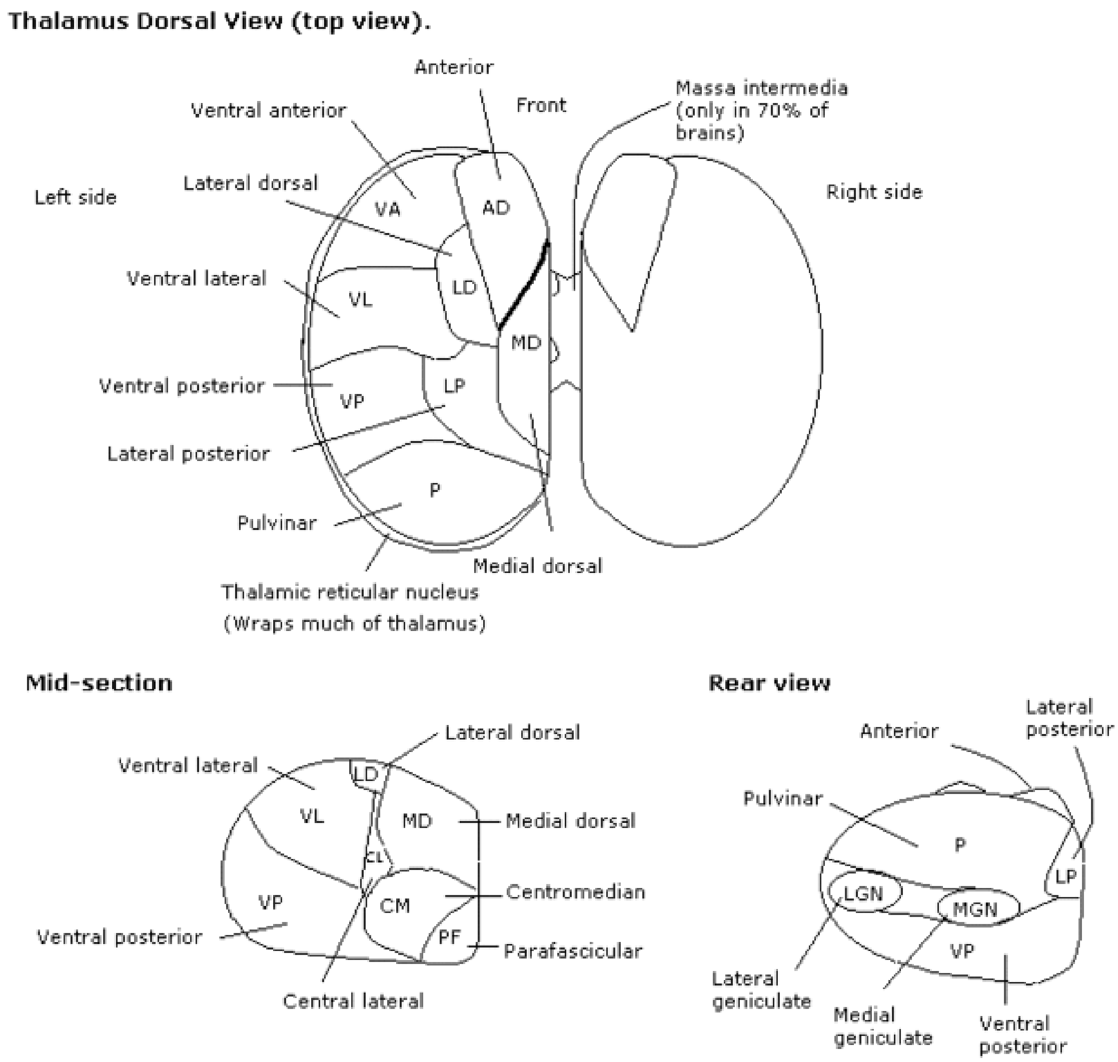
Function in visual perception

The function of the LGN is unknown. It has been shown that while the retina accomplishes spatial decorrelation through center surround inhibition, the LGN accomplishes temporal decorrelation. This spatial-temporal decorrelation makes for much more efficient coding. However, there is almost certainly much more going on.

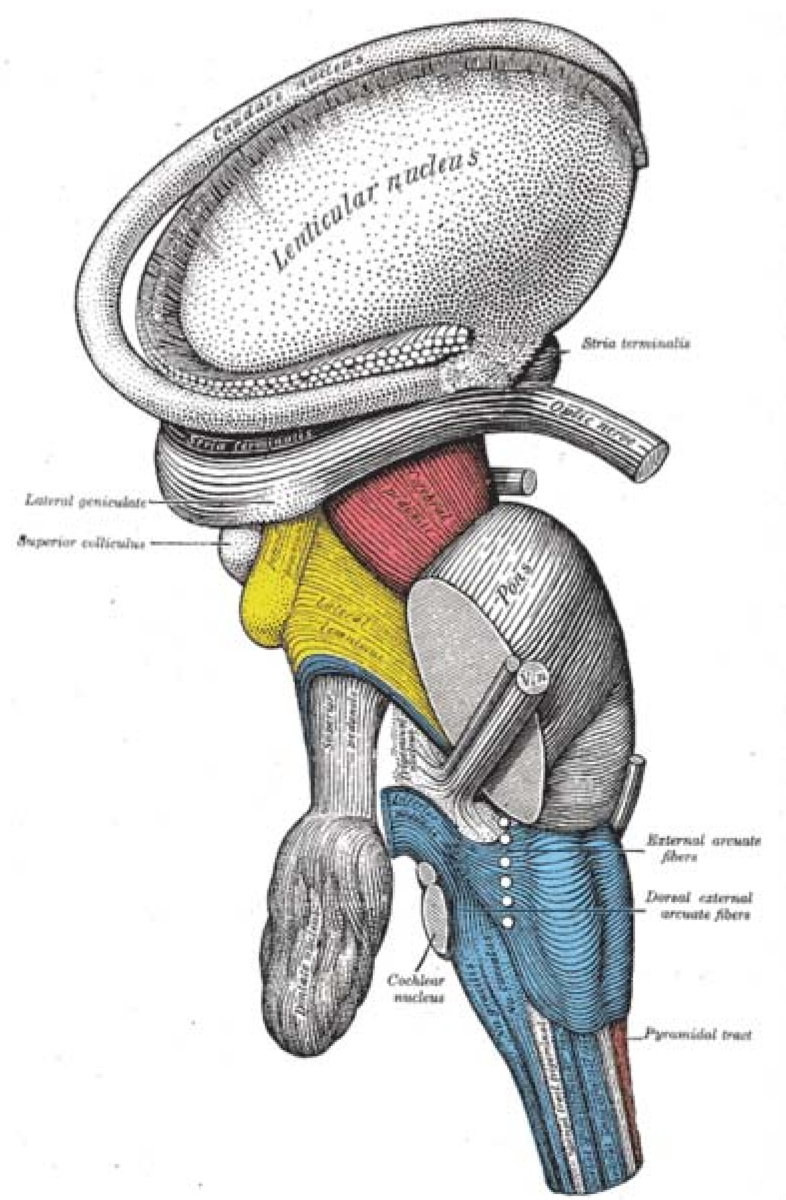
Like other areas of the thalamus, particularly other *relay nuclei*, the LGN likely helps the visual system focus its attention on the most important information. That is, if you hear a sound slightly to your left, the auditory system likely "tells" the visual system, through the LGN, to direct visual attention to that part of space.

The LGN is also a station that refines certain receptive fields.

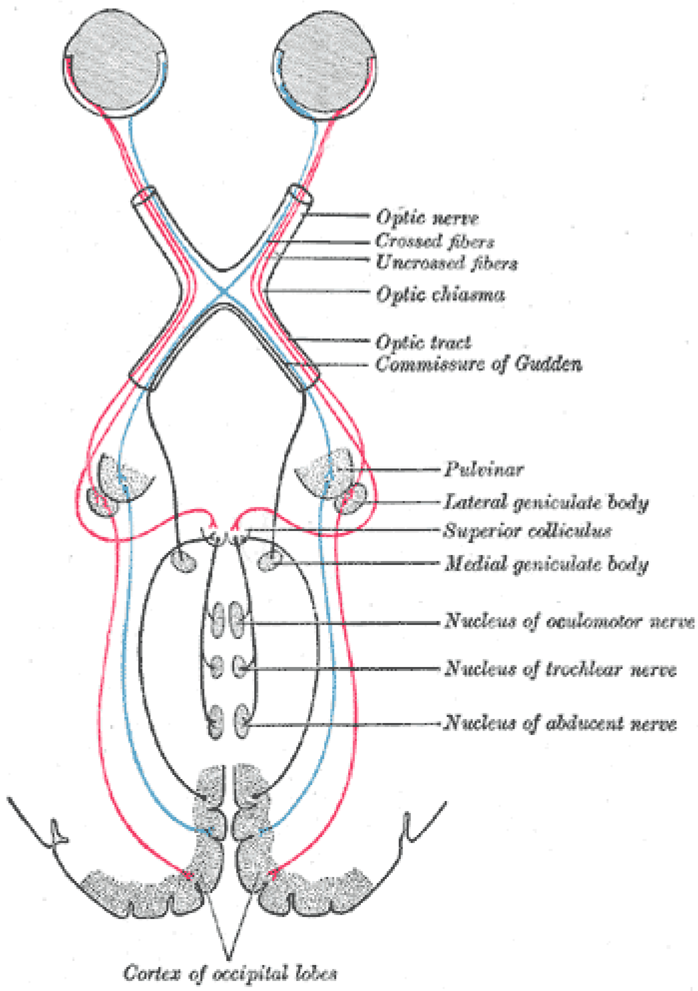
Recent experiments using fMRI in humans have found that both spatial attention and saccadic eye movements can modulate activity in the LGN.


Thalamus Dorsal View (top view).
Anterior
Front
Massa intermedia (only in 70% of brains)
Ventral anterior
Left side
Lateral dorsal
Right side
VA
AD
Ventral lateral
VL
LD
MD
Ventral posterior
LP
VP
Lateral posterior
P
Pulvinar
Medial dorsal
Thalamic reticular nucleus (Wraps much of thalamus)
Mid-section
Lateral dorsal
Ventral lateral
LD
VL
MD
Medial dorsal
CL
VP
CM
Centromedian
PF
Ventral posterior
Parafascicular
Central lateral
Rear view
Lateral posterior
Anterior
Pulvinar
P
LP
LGN
MGN
VP
Lateral geniculate
Medial geniculate
Ventral posterior

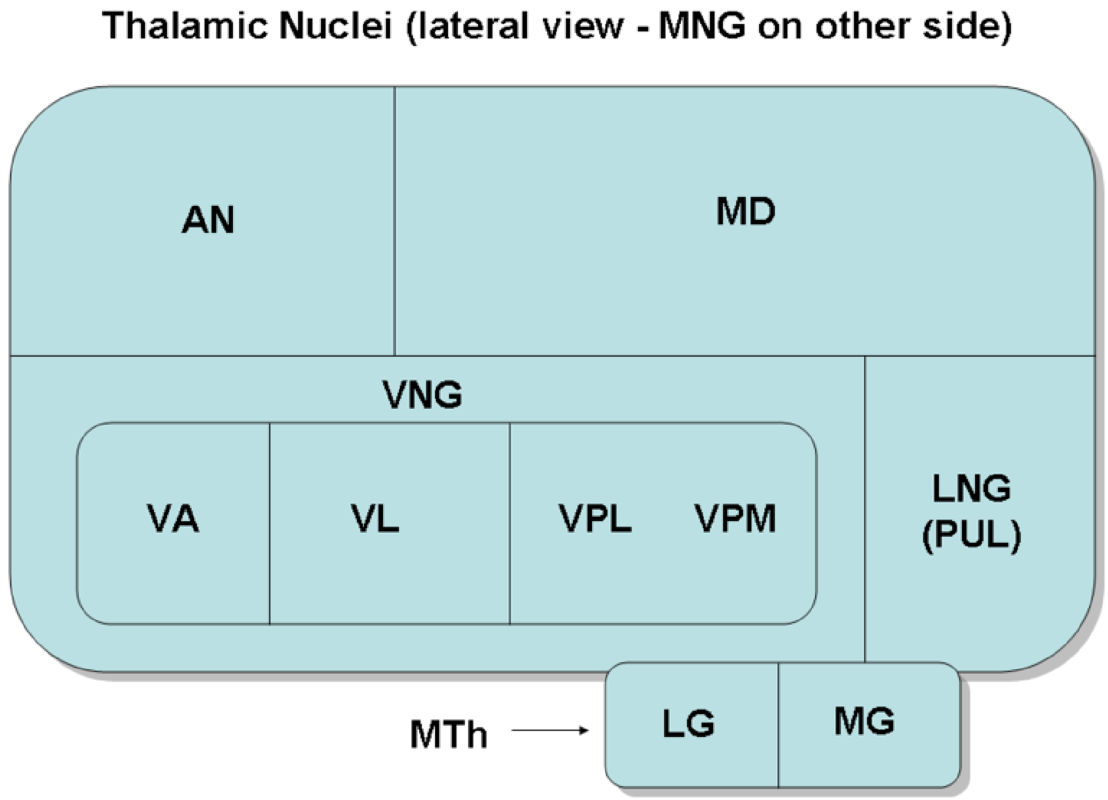
Thalamus



Dissection of brain-stem. Lateral view.



Scheme showing central connections of the optic nerves and optic tracts

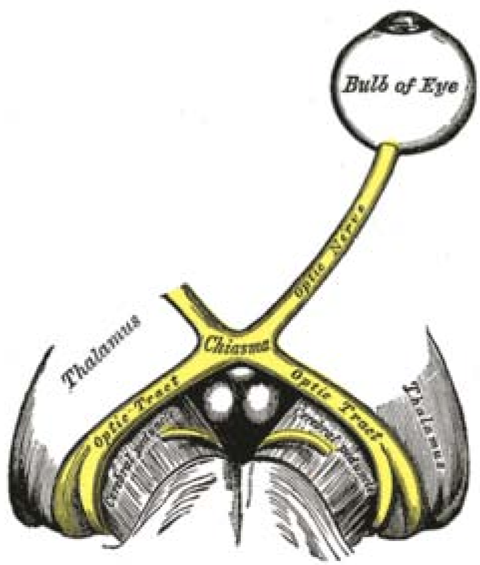


Thalamic nuclei

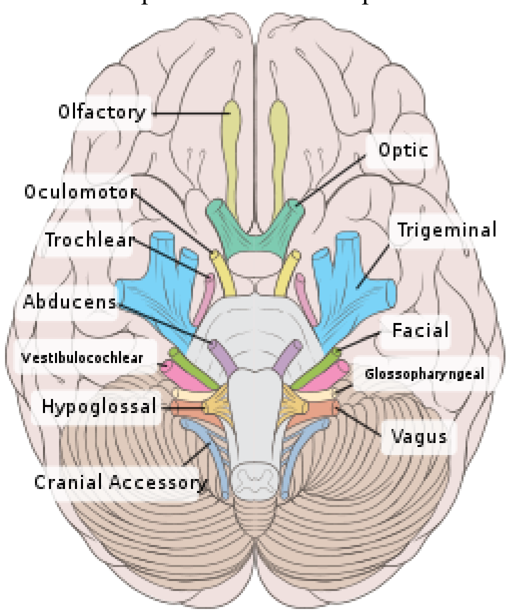
Chapter 18

Optic Nerve

Nerve: Optic Nerve



The left optic nerve and the optic tracts.



Inferior view of the human brain, with the cranial nerves labelled.

Latin	*nervus opticus*
MeSH	*Optic+Nerve*

The **optic nerve**, also called **cranial nerve II**, transmits visual information from the retina to the brain.

Anatomy

The optic nerve is the second of twelve paired cranial nerves but is considered to be part of the central nervous system, as it is derived from an outpouching of the diencephalon during embryonic development. As a consequence, the fibres are covered with myelin produced by oligodendrocytes, rather than Schwann cells, which are found in the peripheral nervous system, and are encased within the meninges. The name "optic nerve" is, in the technical sense, a misnomer, as the optic system lies within the central nervous system and therefore should be named the "optic tract," as nerves exist only, by definition, within the peripheral nervous system. Therefore, peripheral neuropathies like Guillain-Barré syndrome do not affect the optic nerve.

The optic nerve is ensheathed in all three meningeal layers (dura, arachnoid, and pia mater) rather than the epineurium, perineurium, and endoneurium found in peripheral nerves. Fibre tracks of the mammalian central nervous system (as opposed to the peripheral nervous system) are incapable of regeneration, and, hence, optic nerve damage produces irreversible blindness. The fibres from the retina run along the optic nerve to nine primary visual nuclei in the brain, whence a major relay inputs into the primary visual cortex.

The optic nerve is composed of retinal ganglion cell axons and support cells. It leaves the orbit (eye) via the optic canal, running postero-medially towards the optic chiasm, where there is a partial decussation (crossing) of fibres from the nasal visual fields of both eyes. Most of the axons of the optic nerve terminate in the lateral geniculate nucleus from where information is relayed to the visual cortex, while other axons terminate in the pretectal nucleus and are involved in reflexive eye movements. Other axons terminate in the suprachiasmatic nucleus and are involved in regulating the sleep-wake cycle. Its diameter increases from about 1.6 mm within the eye to 3.5 mm in the orbit to 4.5 mm within the cranial space. The optic nerve component lengths are 1 mm in the globe, 24 mm in the orbit, 9 mm in the optic canal, and 16 mm in the cranial space before joining the optic chiasm. There, partial decussation occurs, and about 53% of the fibers cross to form the optic tracts. Most of these fibres terminate in the lateral geniculate body.

From the lateral geniculate body, fibers of the optic radiation pass to the visual cortex in the occipital lobe of the brain. In more specific terms, fibers carrying information from the contralateral superior visual field traverse Meyer's loop to terminate in the lingual gyrus below the calcarine fissure in the occipital lobe, and fibers carrying information from the contralateral inferior visual field terminate more superiorly.

Physiology

The eye's blind spot is a result of the absence of photoreceptors in the area of the retina where the optic nerve leaves the eye.

Each optic nerve contains around 1.2 million nerve fibers, which are axons of the retinal ganglion cells of one retina. In the fovea, which has high acuity, these ganglion cells connect to as few as 5 photoreceptor cells; in other areas of retina, they connect to many thousand photoreceptors.

Role in disease

Damage to the optic nerve typically causes permanent and potentially severe loss of vision, as well as an abnormal pupillary reflex, which is diagnostically important. The type of visual field loss will depend on which portions of the optic nerve were damaged. In general:

- Damage *proximal* to the optic chiasm causes loss of vision in the visual field of the same side only.
- Damage *in* the chiasm causes loss of vision laterally in both visual fields (bitemporal hemianopia). It may occur in large pituitary adenomata.
- Damage *distal* to the chiasm causes loss of vision in one eye but affecting both visual fields: The visual field affected is located on the opposite side of the lesion.

Injury to the optic nerve can be the result of congenital or inheritable problems like Leber's Hereditary Optic Neuropathy, glaucoma, trauma, toxicity, inflammation, ischemia, infection (very rarely), or compression from tumors or aneurysms. By far, the three most common injuries to the optic nerve are from glaucoma, optic neuritis (especially in those younger than 50 years of age), and anterior ischemic optic neuropathy (usually in those older than 50).

Glaucoma is a group of diseases involving loss of retinal ganglion cells causing optic neuropathy in a pattern of peripheral vision loss, initially sparing central vision.

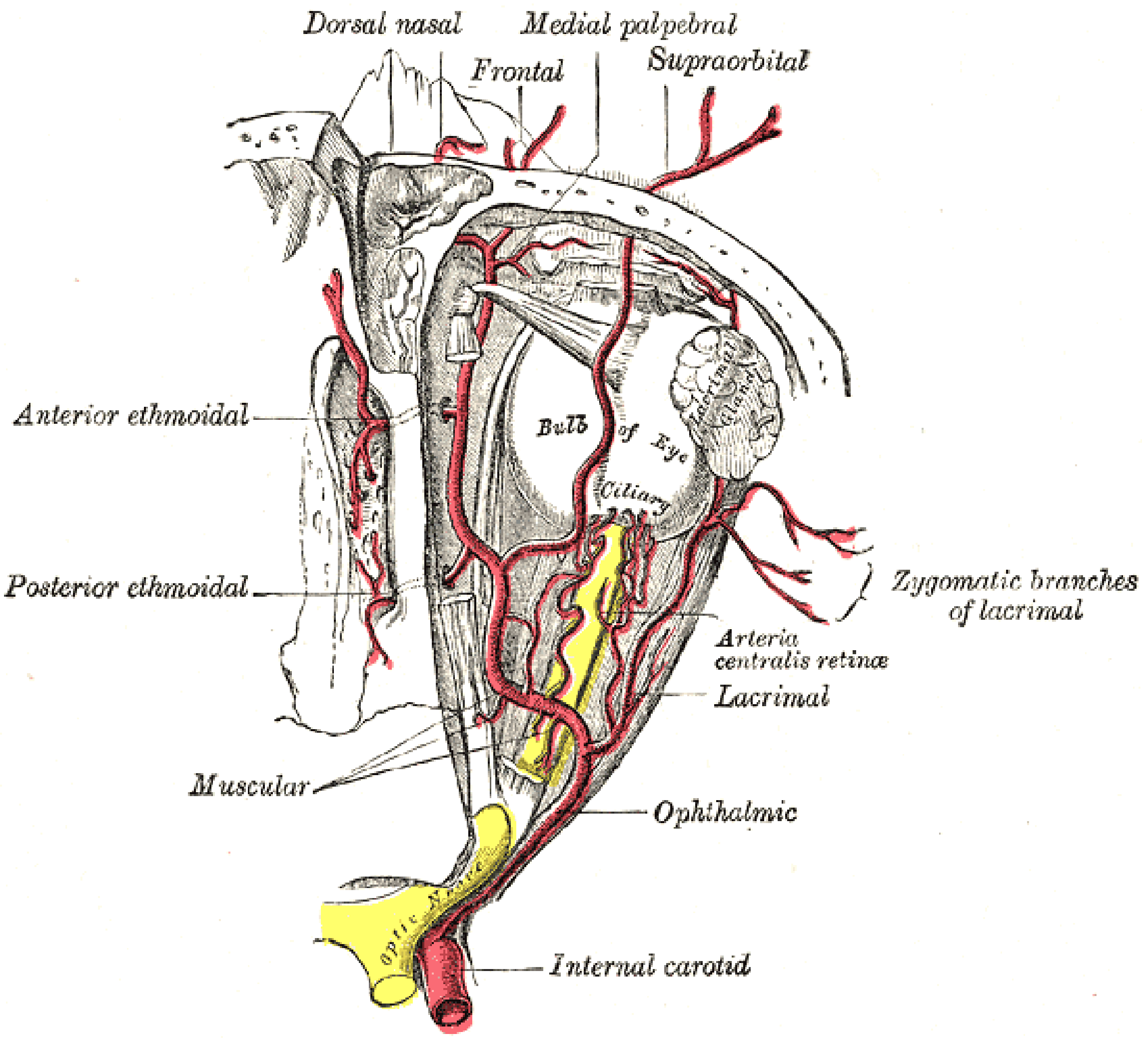
Optic neuritis is inflammation of the optic nerve. It is associated with a number of diseases, the most notable one being multiple sclerosis.

Anterior Ischemic Optic Neuropathy is a particular type of infarct that affects patients with an anatomical predisposition and cardiovascular risk factors.

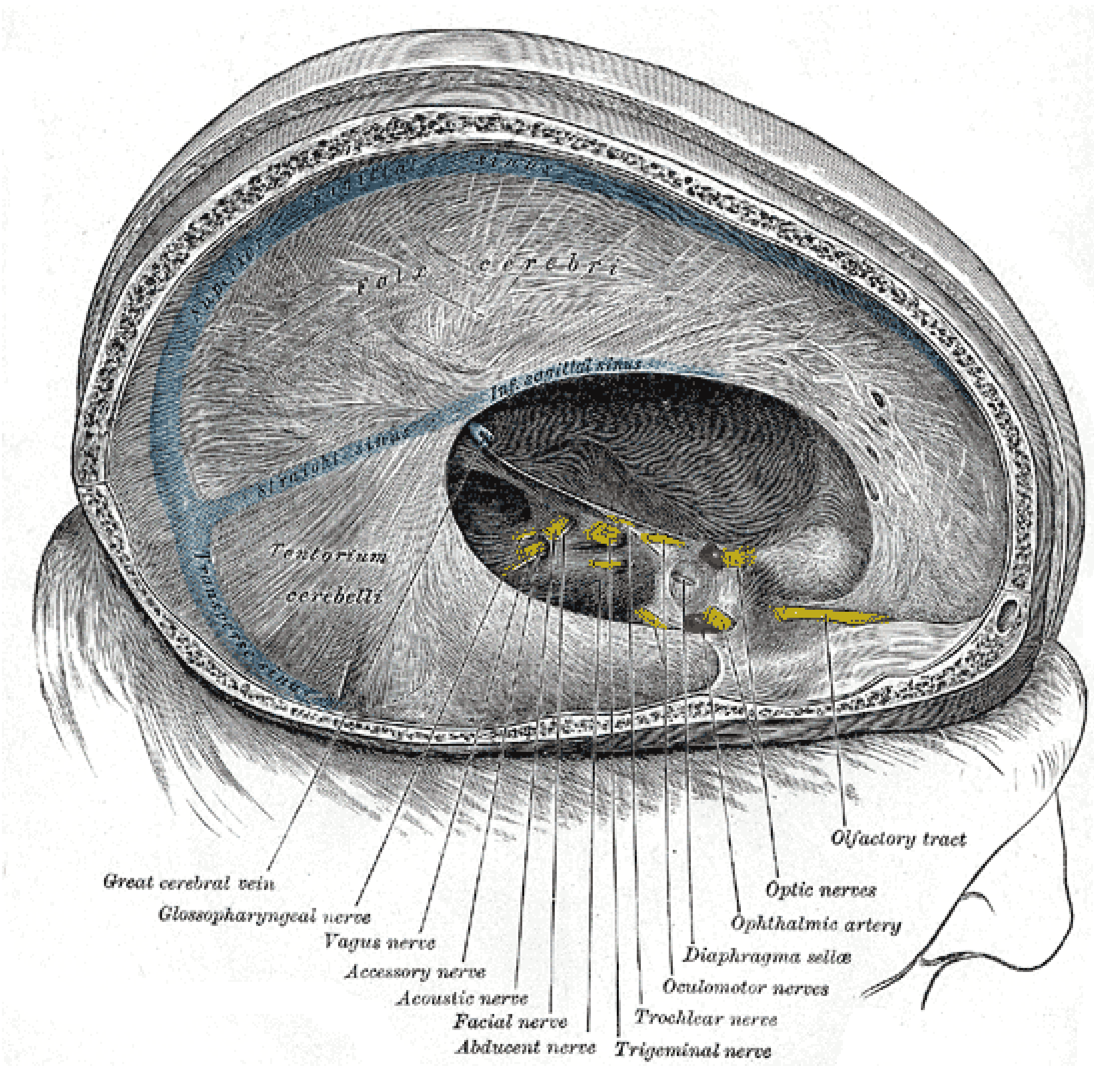
Optic nerve hypoplasia is the under-development of the optic nerve causing little to no vision in the affected eye.

Ophthalmologists, in particular, those sub-specialists that are neuro-ophthalmologists, are often best suited to diagnose and treat diseases of the optic nerve.

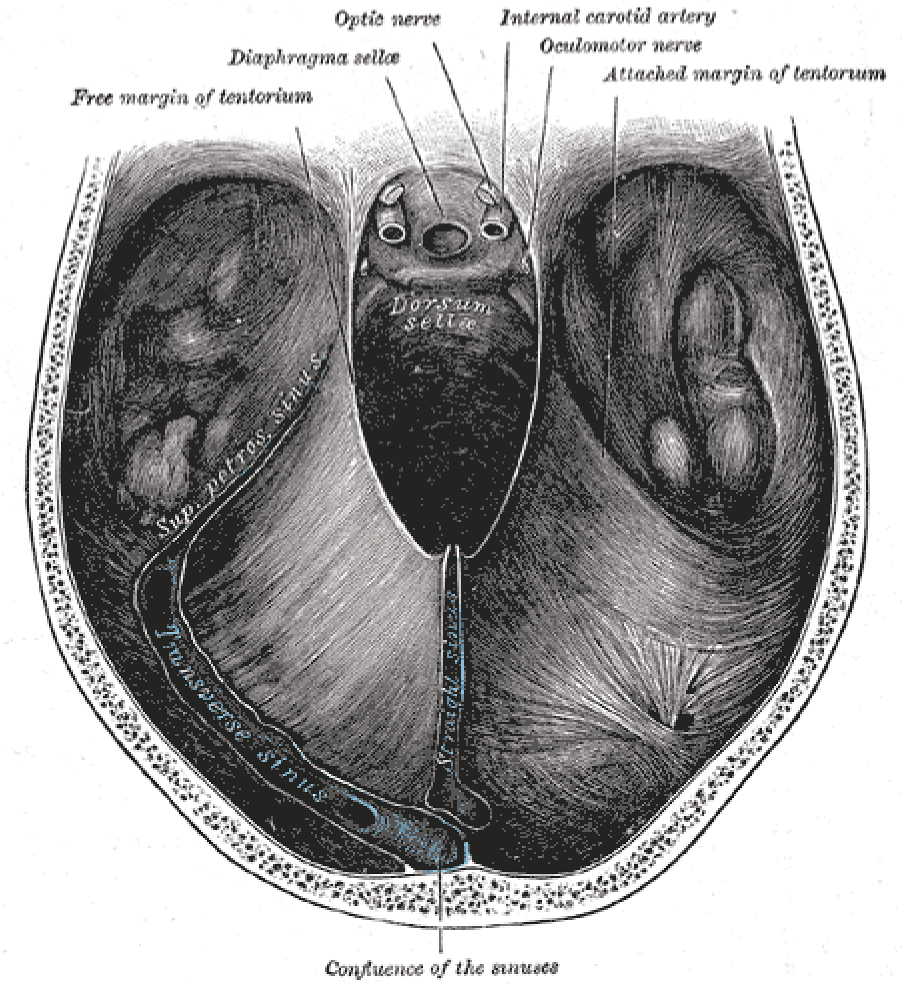
The International Foundation for Optic Nerve Diseases IFOND sponsors research and information on a variety of optic nerve disorders and may provide general direction.



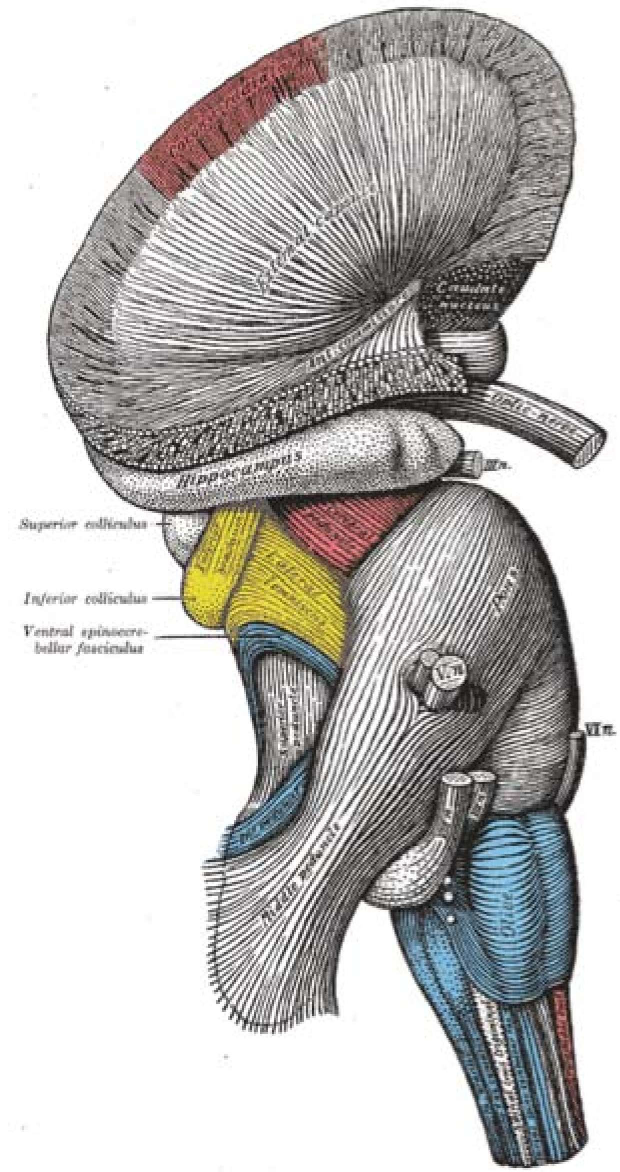
The ophthalmic artery and its branches. (optic nerve is yellow)



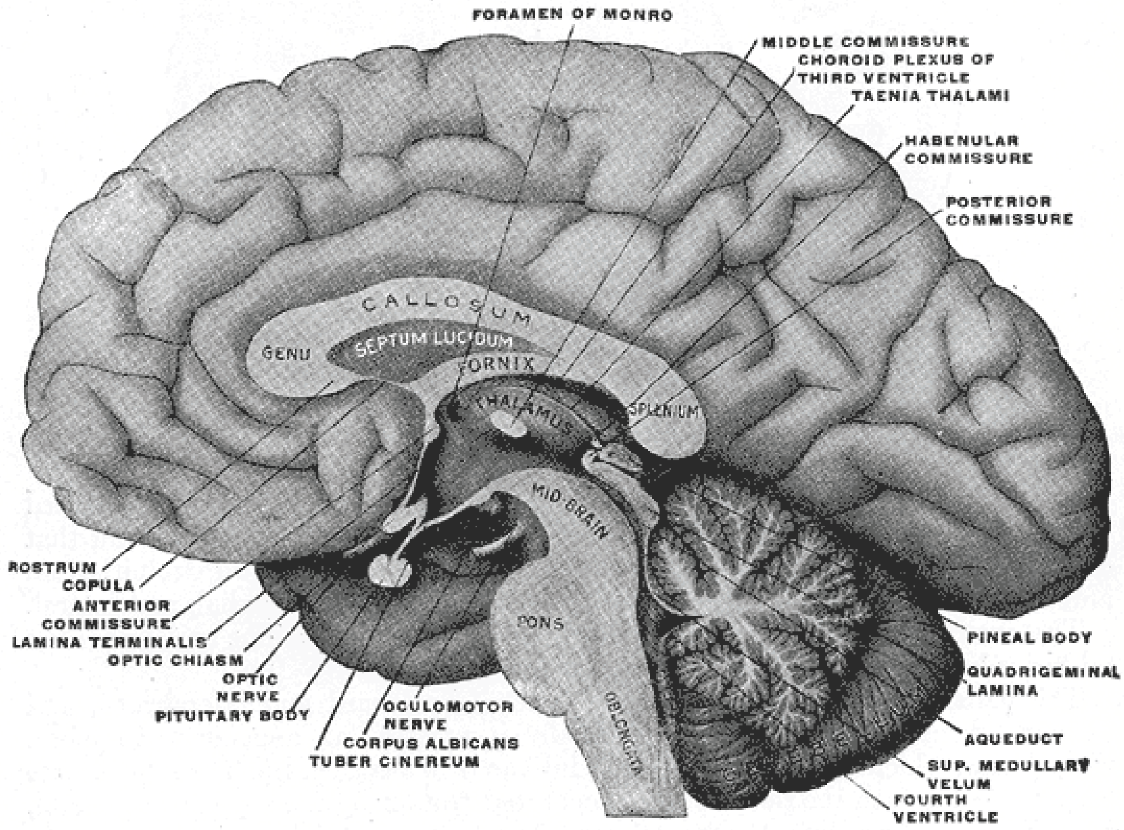
Dura mater and its processes exposed by removing part of the right half of the skull, and the brain.



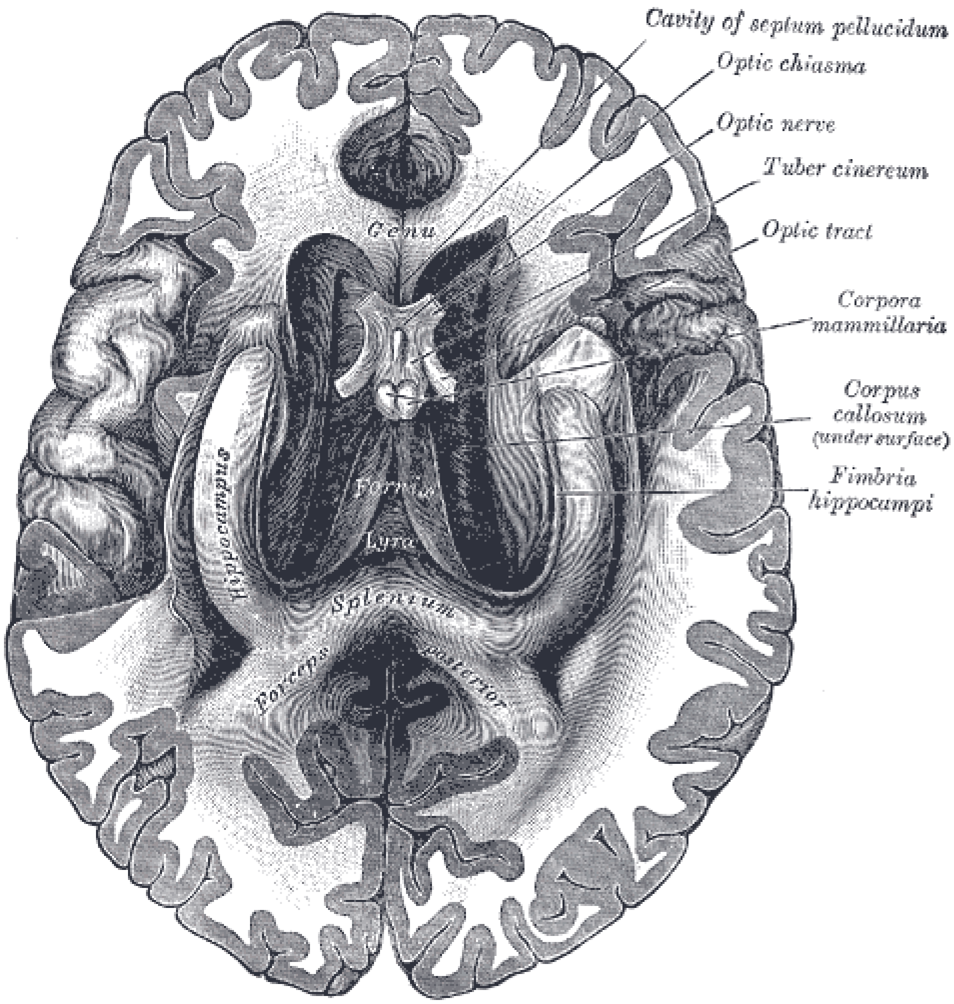
Tentorium cerebelli from above



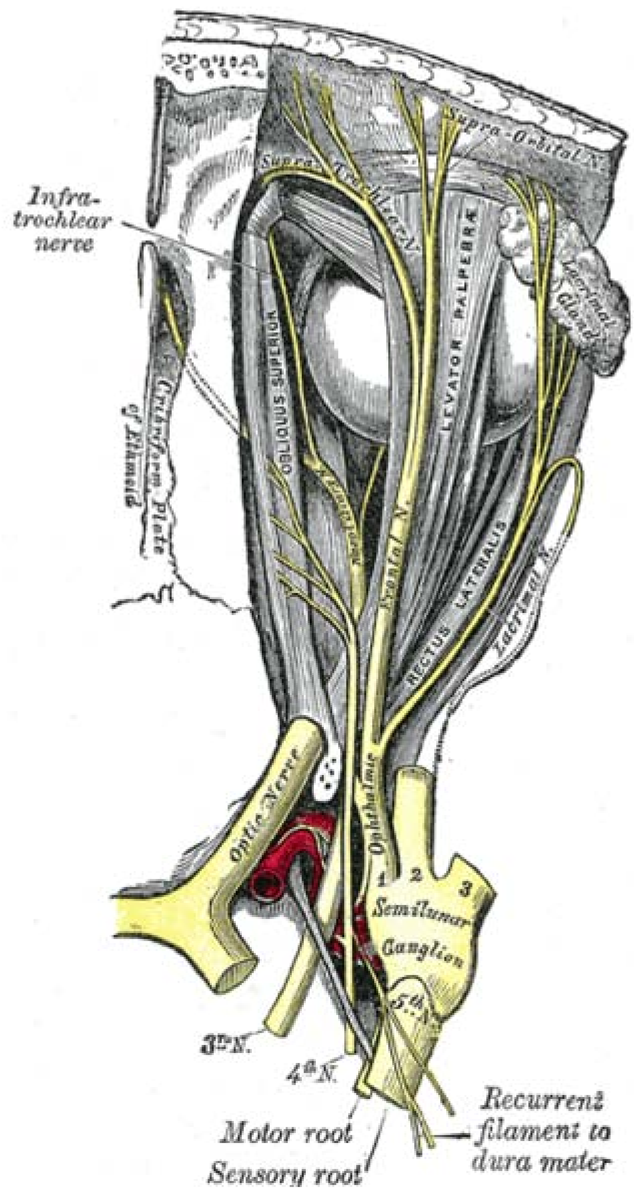
Superficial dissection of brain-stem. Lateral view.



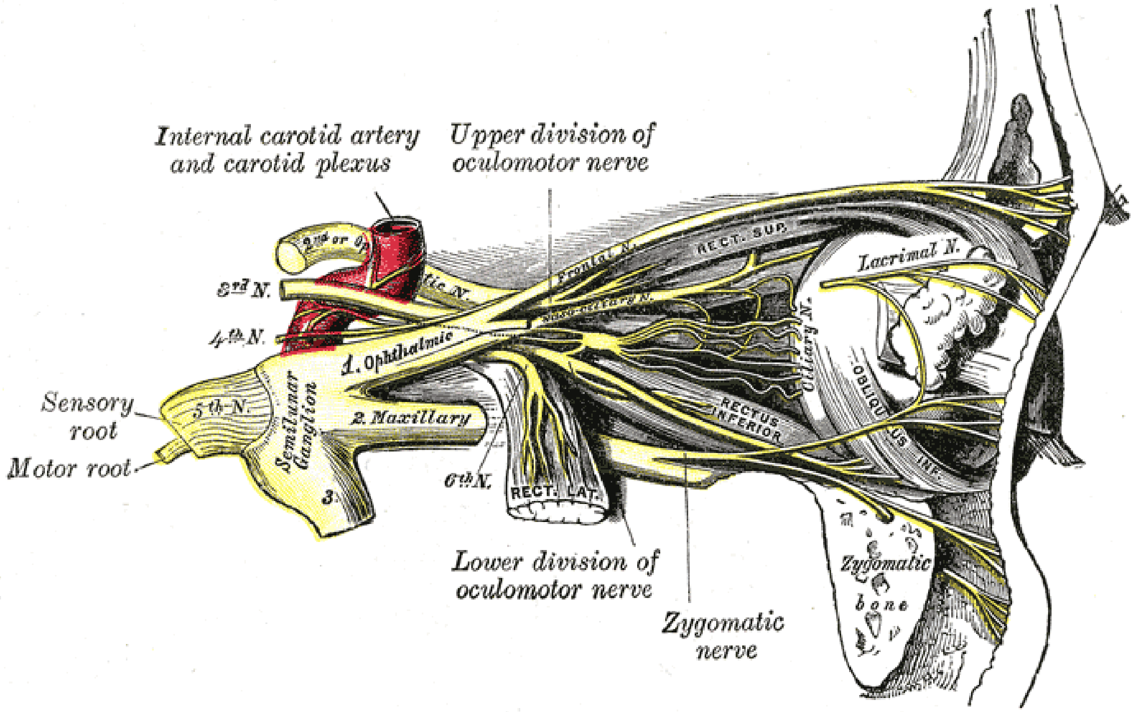
Mesal aspect of a brain sectioned in the median sagittal plane.



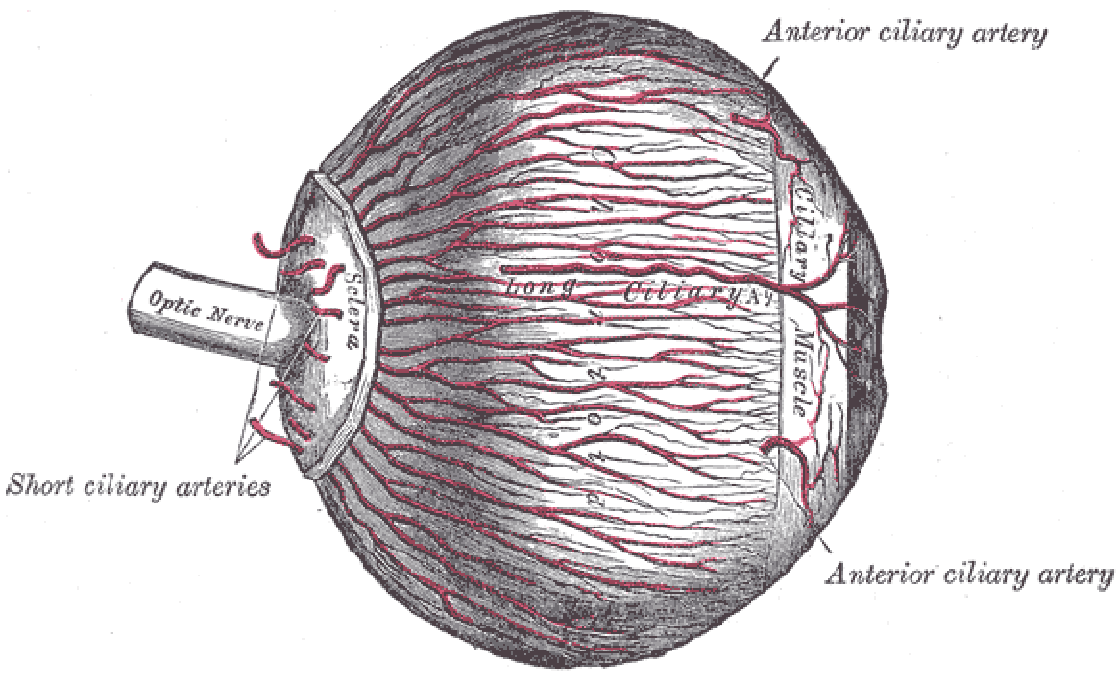
The fornix and corpus callosum from below



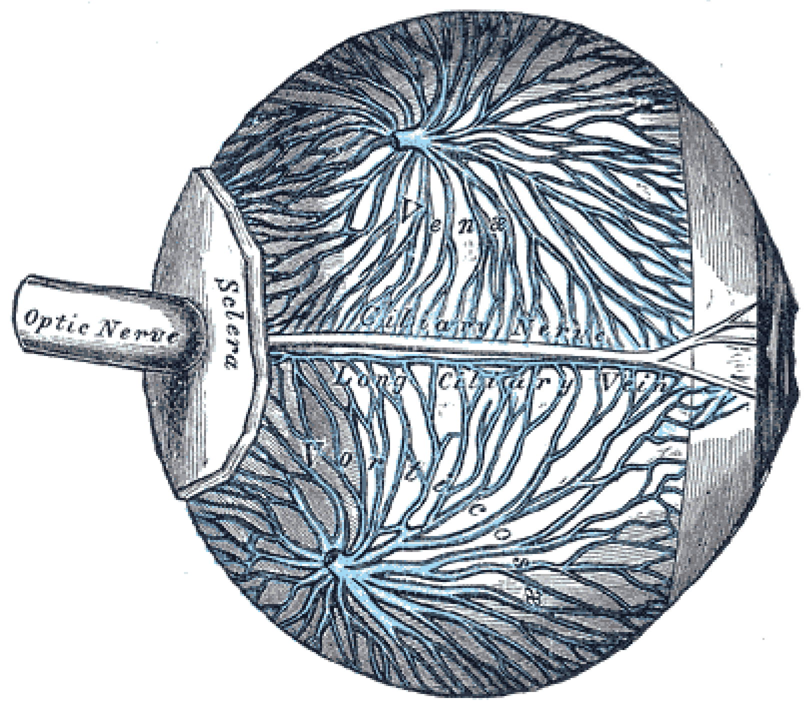
Nerves of the orbit. Seen from above.



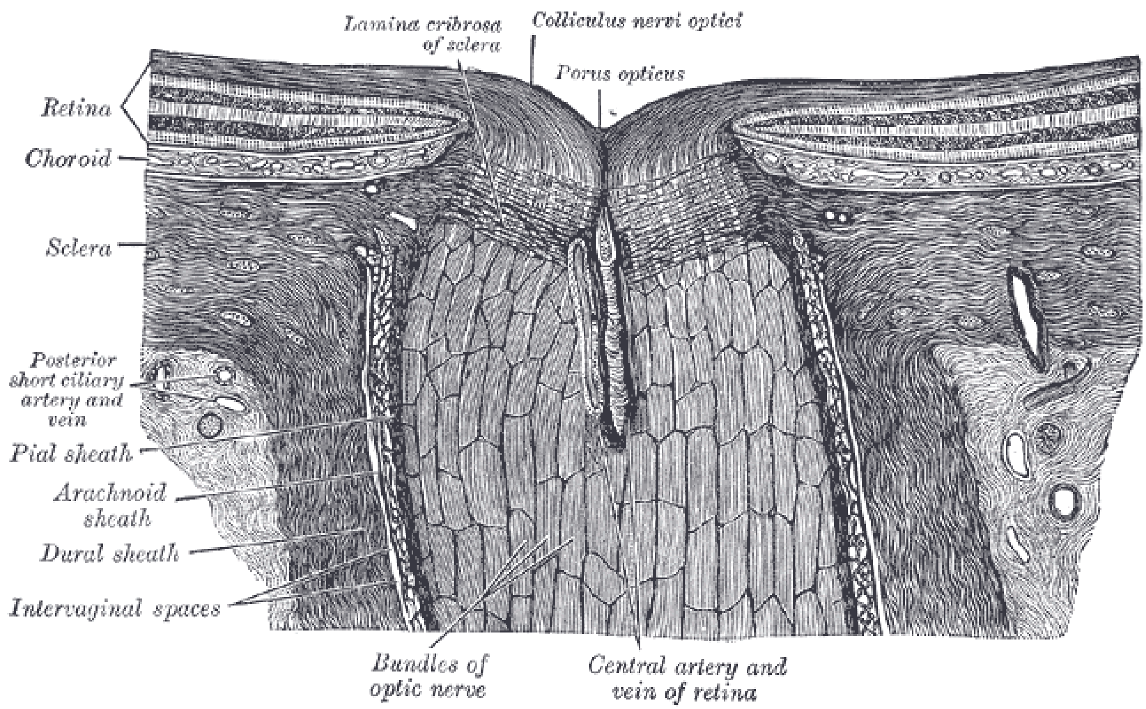
Nerves of the orbit, and the ciliary ganglion. Side view.



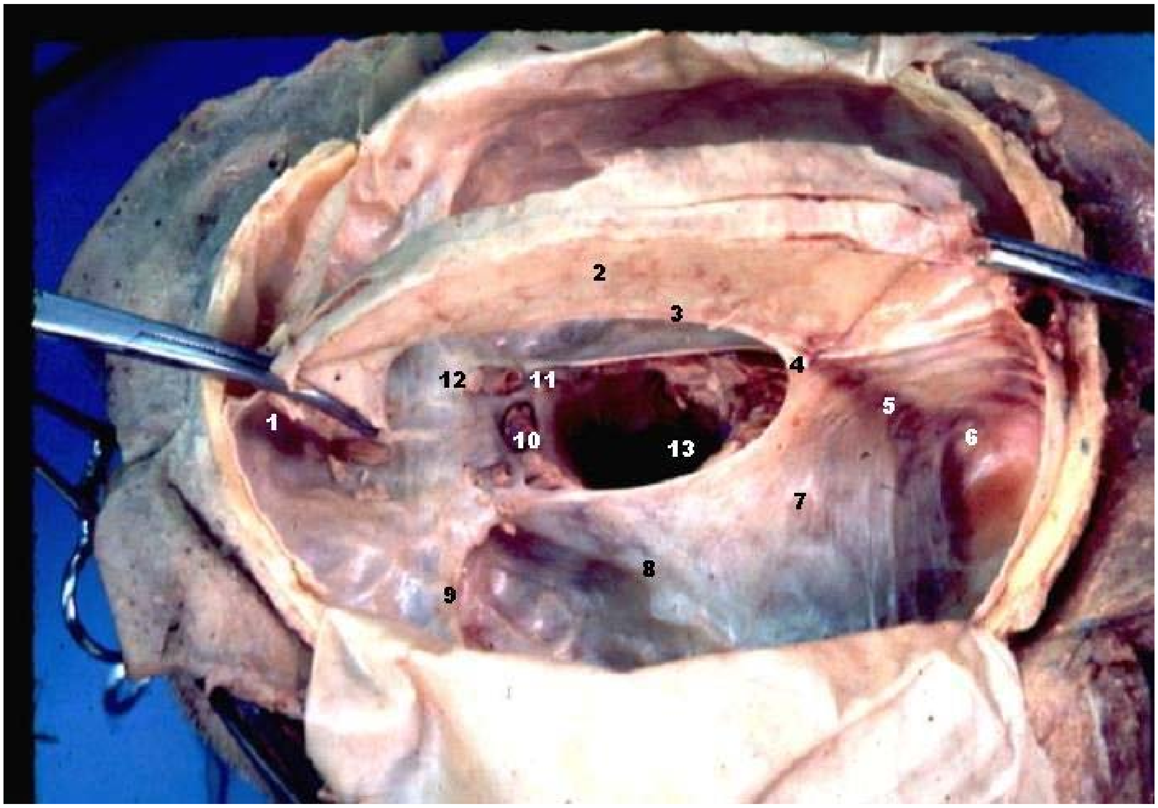
The arteries of the choroid and iris. The greater part of the sclera has been removed.



The veins of the choroid



The terminal portion of the optic nerve and its entrance into the eyeball, in horizontal section.



Human brain dura mater (reflections)

MRI scan of human eye showing optic nerve

Chapter 19

Retinal Ganglion Cell

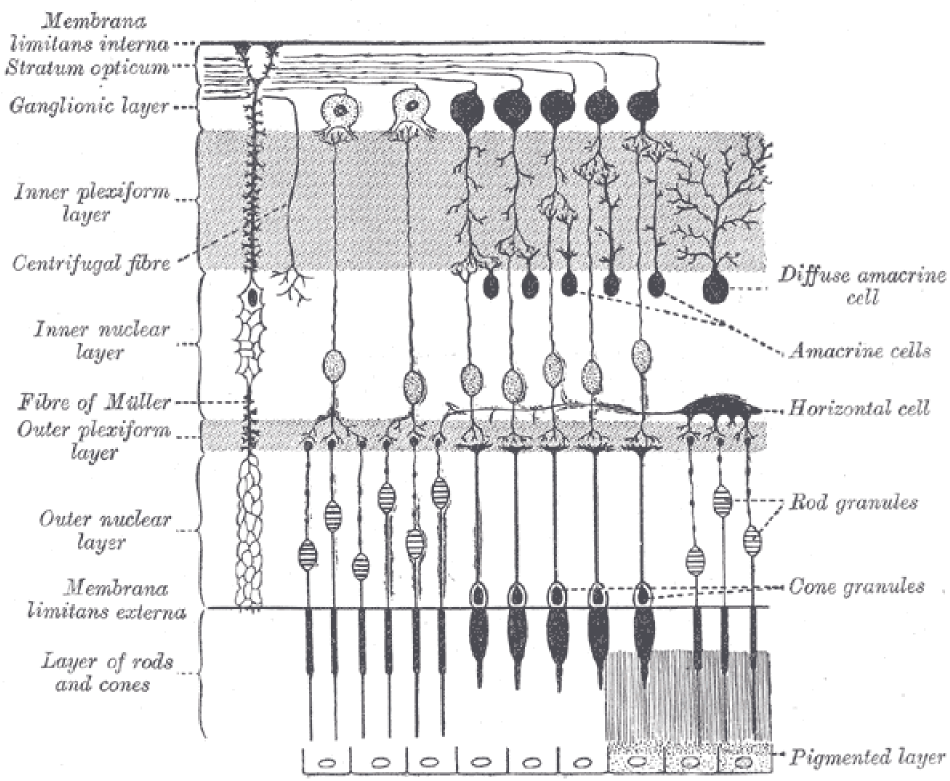


Diagram showing cross-section of retinal layers. The area labeled "Ganglionic layer" contains retinal ganglion cells.

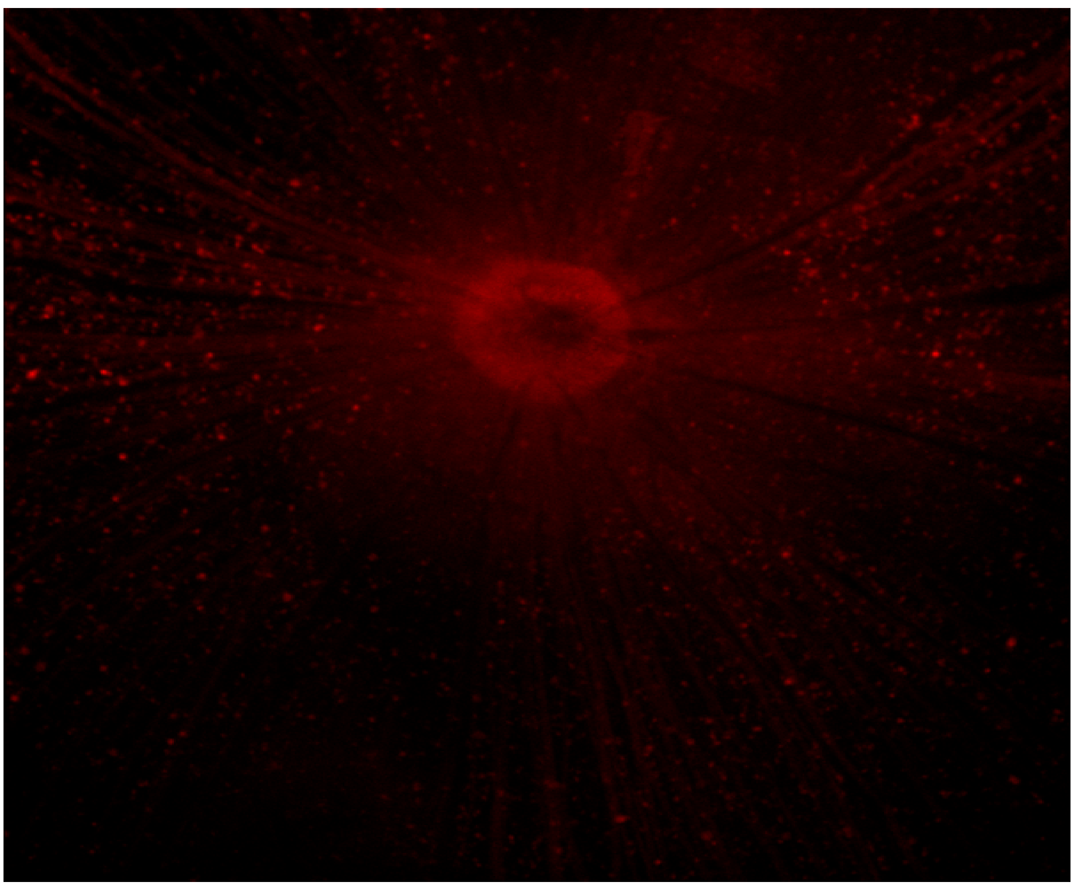
A **retinal ganglion cell** (RGC) is a type of neuron located near the inner surface (the ganglion cell layer) of the retina of the eye. It receives visual information from photoreceptors via two intermediate neuron types: bipolar cells and amacrine cells. Retinal ganglion cells collectively transmit image-forming and non-image forming visual information from the retina to several regions in the thalamus, hypothalamus, and mesencephalon, or midbrain.

Retinal ganglion cells vary significantly in terms of their size, connections, and responses to visual stimulation but they all share the defining property of having a long axon that extends into the brain. These axons form the optic nerve, optic chiasm, and optic tract. A small percentage of retinal ganglion cells contribute little or nothing to vision, but are themselves photosensitive; their axons form the retinohypothalamic tract and contribute to circadian rhythms and pupillary light reflex, the resizing of the pupil.

Function

There are about 1.2 to 1.5 million retinal ganglion cells in the human retina. With about 125 million photoreceptors per retina, on average each retinal ganglion cell receives inputs from about 100 rods and cones. However, these numbers vary greatly among individuals and as a function of retinal location. In the fovea (center of the retina), a single ganglion cell will communicate with as few as five photoreceptors. In the extreme periphery (ends of the retina), a single ganglion cell will receive information from many thousands of photoreceptors.

Retinal ganglion cells spontaneously fire action potentials at a base rate while at rest. Excitation of retinal ganglion cells results in an increased firing rate while inhibition results in a depressed rate of firing.



A false-color image of a flat-mounted rat retina viewed through a fluorescence microscope at 50x magnification. The optic nerve was injected with a fluorophore, causing retinal ganglion cells to fluoresce.

Types

Based on their projections and functions, there are at least five main classes of retinal ganglion cells:

- Midget cell (Parvocellular, or P pathway; B cells)
- Parasol cell (Magnocellular, or M pathway; A cells)
- Bistratified cell (Koniocellular, or K pathway)
- Photosensitive ganglion cells
- Other ganglion cells projecting to the superior colliculus for eye movements (saccades)

Midget

Midget retinal ganglion cells project to the parvocellular layers of the lateral geniculate nucleus. These cells are known as midget retinal ganglion cells, based on the small sizes of their dendritic trees and cell bodies. About 80% of all retinal ganglion cells are midget cells in the parvocellular pathway. They receive inputs from relatively few rods and cones. In many cases, they are connected to midget bipolars, which are linked to one cone each. They have slow conduction velocity, and respond to changes in color but respond only weakly to changes in contrast unless the change is great (Kandel et al., 2000). They have simple center-surround receptive fields, where the center may be either ON or OFF while the surround is the opposite.

Parasol

Parasol retinal ganglion cells project to the magnocellular layers of the lateral geniculate nucleus. These cells are known as parasol retinal ganglion cells, based on the large sizes of their dendritic trees and cell bodies. About 10% of all retinal ganglion cells are parasol cells, and these cells are part of the magnocellular pathway. They receive inputs from relatively many rods and cones. They have fast conduction velocity, and can respond to low-contrast stimuli, but are not very sensitive to changes in color (Kandel et al., 2000). They have much larger receptive fields which are nonetheless also center-surround.

Bistratified

Bistratified retinal ganglion cells project to the koniocellular layers of the lateral geniculate nucleus. Bistratified retinal ganglion cells have been identified only relatively recently. Koniocellular means “cells as small as dust”; their small size made them hard to find. About 10% of all retinal ganglion cells are bistratified cells, and these cells go through the koniocellular pathway. They receive inputs from intermediate numbers of rods and cones. They have moderate spatial resolution, moderate conduction velocity, and can respond to moderate-contrast stimuli. They may be involved in color vision. They have very large receptive fields that only have centers (no surrounds) and are always ON to the blue cone and OFF to both the red and green cone.

Photosensitive ganglion cell

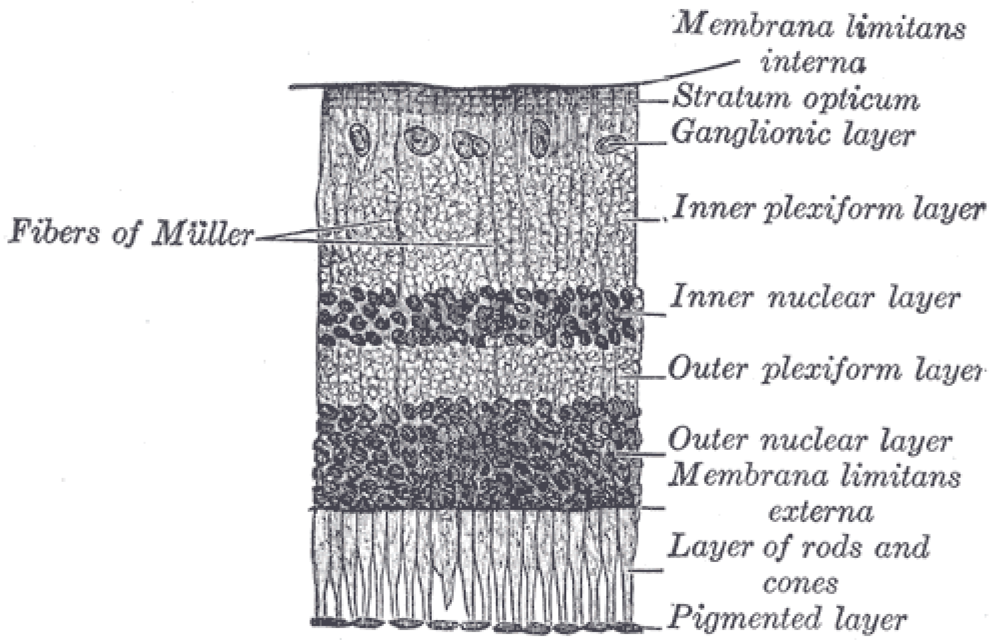
Photosensitive ganglion cells, including but not limited to the giant retinal ganglion cells, contain their own photopigment, melanopsin, which makes them respond directly to light even in the absence of rods and cones. They project to, among other areas, the suprachiasmatic nucleus (SCN) via the retinohypothalamic tract for setting and maintaining circadian rhythms. Other retinal ganglion cells projecting to the lateral geniculate nucleus (LGN) include cells making connections with the Edinger-Westphal nucleus (EW), for control of the pupillary light reflex, and giant retinal ganglion cells.

Retinal ganglion cell physiology

Most mature ganglion cells are able to fire action potentials at a high frequency because of their expression of K_v3 potassium channels.

Chapter 20

Photosensitive Ganglion Cell



Section of retina: light strikes first the ganglion cell layer, last the rods and cones

Photosensitive ganglion cells, also called **photosensitive Retinal Ganglion Cells** (pRGC), **intrinsically photosensitive Retinal Ganglion Cells** (ipRGC) or **melanopsin-containing ganglion cells**, are a type of neuron (nerve cell) in the retina of the mammalian eye. They were discovered in the early 1990s and are, unlike other retinal ganglion cells, intrinsically photosensitive. This means that they are a third class of retinal photoreceptors, excited by light even when all influences from classical photoreceptors (rods and cones) are blocked (either by applying pharmacological agents or by dissociating the ganglion cell from the retina). Photosensitive ganglion cells contain the photopigment melanopsin. The giant retinal ganglion cells of the primate retina are examples of photosensitive ganglion cells.

Brief overview

Compared to the rods and cones, the ipRGC respond more sluggishly and signal the presence of light over the long term. They represent a small subset (~1-3%) of the retinal ganglion cells. Their functional roles are non-image-forming and fundamentally different from those of pattern vision; they provide a stable representation of ambient light intensity. They have at least three primary functions.

- They play a major role in synchronizing circadian rhythms to the 24-hour light/dark cycle, providing primarily length-of-day and length-of night information. They send light information via the retinohypothalamic tract directly to the circadian pacemaker of the brain, the suprachiasmatic nucleus of the hypothalamus. The physiological properties of these ganglion cells match known properties of the daily light entrainment (synchronization) mechanism regulating circadian rhythms.

- Photosensitive ganglion cells innervate other brain targets, such as the center of pupillary control, the olivary pretectal nucleus of the midbrain. They contribute to the regulation of pupil size and other behavioral responses to ambient lighting conditions.

- They contribute to photic regulation of, and acute photic suppression of, release of the hormone melatonin from the pineal gland.

Photosensitive ganglion cells are also responsible for the persistence of circadian and pupillary light responses in mammals with degenerated rod and cone photoreceptors, such as humans suffering from retinitis pigmentosa.

Recently photoreceptive ganglion cells have been isolated in humans where, in addition to the above functions shown in other mammals, they have been shown to mediate a degree of light recognition in rodless, coneless subjects suffering with disorders of rod and cone photoreceptors. Work by Farhan H. Zaidi and colleagues showed that photoreceptive ganglion cells may have a visual function and can be isolated in humans.

The photopigment of photoreceptive ganglion cells, melanopsin, is excited by light mainly in the blue portion of the visible spectrum (absorption peaks at ~480 nanometers). The phototransduction mechanism in these cells is not fully understood, but seems likely to resemble that in invertebrate rhabdomeric photoreceptors. Photosensitive ganglion cells respond to light by depolarizing and increasing the rate at which they fire nerve impulses. In addition to responding directly to light, these cells may receive excitatory and inhibitory influences from rods and cones by way of synaptic connections in the retina.

Discovery

In 1991 Russell G. Foster and colleagues including Ignacio Provencio discovered a non-rod, non-cone photoreceptor in the eyes of mice where it was shown to mediate circadian rhythms, i.e. the body's 24-hour biological clock. Foster was elected a fellow of the Royal Society in 2008. The fact that such a landmark discovery was published in a relatively obscure science journal indicates the initial skepticism within the scientific community about the existence of non-rod, non-cone photoreceptors. That community continued for several years to believe that the only photoreceptors were rods and cones as if this were written in stone - and why not, after all, as Foster himself notes, the eye had been the subject of detailed study for a continuous period of over 200 years, so at the time it seemed unlikely that great minds since Newton, Maxwell, through to Einstein and beyond, could have missed this receptor's existence, its functions, and its ramifications. But miss it they did and it fell to contemporary researchers to make the landmark discoveries in the field, ground-breaking discoveries that still continue to be made. These novel cells express the photopigment melanopsin which was first identified by Provencio and colleagues who published in the Journal of Neuroscience in 2000. Major advances in the field would henceforth only be published in major biology and science journals, reflecting the gradual acceptance of the novel receptor by the scientific community.

Melanopsin absorbs different maximal wavelength

Robert Lucas and colleagues including Russell Foster were the first to show conclusively that cells containing the photopigment melanopsin absorb light maximally at a different wavelength than those of rods and cones. Lucas, Foster and colleagues also discovered that in mice the non-rod, non-cone photoreceptor had a role in initiating the pupil light reflex and not only circadian / behavioural functions as previously thought, though the latter were also demonstrated by them using genetically engineered rodless, coneless mice. Samer Hattar and colleagues including David Berson in 2002 showed that in the rat, intrinsically photosensitive retinal ganglion cells invariably expressed melanopsin, and so melanopsin (and not rod or cone opsins) was most likely the visual pigment of phototransducing retinal ganglion cells that set the circadian clock and initiated other non-image-forming visual functions. This work is regarded by Current Biology, New Scientist and various other commentators as representing the discovery that the identity of the non-rod, non-cone photoreceptor in mice was a class of retinal ganglion cells (RGCs). This was highly significant anatomically; ganglion cells reside in the inner retina, while classic photoreceptors (rods and cones) inhabit the outer retina. There are thus two parallel and anatomically distinct photoreceptor pathways.

In the same year, 2005, Melyan and Qiu together with colleagues including Lucas, Mark W. Hankins and Berson, showed that the melanopsin photopigment was the phototransduction pigment in ganglion cells. Dennis Dacey with colleagues including Paul Gamlin showed in a species of Old World monkey that giant ganglion cells expressing melanopsin projected to the lateral geniculate nucleus (LGN). Previously only projections to the midbrain (pre-tectal nucleus) and hypothalamus (supra-chiasmatic nuclei, SCN) had been shown. However a visual role for the receptor was still unsuspected and unproven.

Research in humans

Attempts were made to hunt down the receptor in humans. But humans posed special challenges and demanded a new model - for unlike in animals, extensive ethical issues meant rod and cone loss could not be induced genetically or with chemicals so as to directly study the ganglion cells. For many years, only inferences could be drawn about the receptor in humans, though these were at times pertinent.

In 2007 the breakthrough came when Zaidi and colleagues including Foster, George Brainard, Charles Czeisler and Steven Lockley, having teamed up with other researchers on both sides of the Atlantic, published their pioneering work using rodless, coneless humans. *Current Biology* subsequently announced in their 2008 editorial, commentary and despatches to scientists and ophthalmologists, that the non-rod, non-cone photoreceptor had been conclusively discovered in humans using landmark experiments on rodless, coneless humans by Zaidi and colleagues. The 2007 discovery of the novel receptor in humans, as well as the spectacular discovery, made alongside, that it mediated conscious sight, was trumpeted by *Cell Press, New Scientist,* and other science commentators in 2007. The identity of the non-rod, non-cone photoreceptor in humans was found to be a ganglion cell in the inner retina exactly as previously shown in rodless, coneless models in some other mammals. The work was done using patients with rare diseases that wiped out classic rod and cone photoreceptor function but preserved ganglion cell function. Despite having no rods or cones, the patients continued to exhibit circadian photoentrainment, circadian behavioural patterns, melatonin suppression, and pupil reactions, with peak spectral sensitivities to environmental and experimental light matching that for the melanopsin photopigment. Their brains could also associate vision with light of this frequency. Jacob Schor comments that in addition to being an outstanding example of collaboration between different countries, as well as between clinicians and scientists, interest thenceforth started to be shown by clinicians including ophthalmologists with a view to understanding the new receptor's role in human diseases and as discussed below, blindness.

New role in conscious sight

The use of rodless, coneless humans allowed another possible role for the receptor to be studied. In 2007, a new role was found for the photoreceptive ganglion cell. Zaidi and colleagues including Foster, Brainard, Czeisler and Lockley, showed that, at least in humans, the retinal ganglion cell photoreceptor contributes to conscious sight as well as to non-image-forming functions like circadian rhythms, behaviour and pupillary reactions. Humans were the perfect model in which to prove this function as they can describe sight readily to an observer, which animals cannot do. Hence the receptor by its location anatomically in the inner retina as shown by these researchers was the first cell to perceive light giving rise to vision. Since these cells respond mostly to blue light, it has been suggested that they have a role in mesopic vision and that the old theory of a purely duplex retina with rod (dark) and cone (light) light vision was simplistic. Zaidi and colleagues' work with rodless, coneless human subjects hence also opened the door into image-forming (visual) roles for the ganglion cell photoreceptor.

The discovery that there are parallel pathways for vision was made - one classic rod and cone-based arising from the outer retina, the other a rudimentary visual brightness detector arising from the inner retina and which seems to be activated by light before the other. Classic photoreceptors also feed into the novel photoreceptor system, and colour constancy may be an important role as suggested by Foster. Like many of the key discoveries about the new receptor, the work by Zaidi and colleagues shatters hundreds of years of what science thought it knew about the most basic functions of the eye and vision.

The authors on the rodless, coneless human model summarised their landmark paper noting for the first time that the receptor could be instrumental in understanding many diseases including major causes of blindness worldwide such as glaucoma, a disease which affects ganglion cells. Study of the receptor offered potential as a new avenue to explore in trying to find treatments for blindness. It is in these discoveries of the novel photoreceptor in humans and in the receptor's role in vision, rather than its non-image-forming functions, where the receptor may have the greatest impact on society as a whole, though the impact of disturbed circadian rhythms is another area of relevance to clinical medicine.

Violet-to-blue light

Most work suggests that the peak spectral sensitivity of the receptor is between 460 and 484 nm. Lockley et al. in 2003 showed that 460 nm (violet) wavelengths of light suppress melatonin twice as much as 555 nm (green) light, the peak sensitivity of the photopic visual system. However, in more recent work by Zaidi, Lockley and co-authors using a rodless, coneless human, it was found that what consciously led to light perception was a very intense 481 nm stimulus; this means that the receptor in visual terms enables some rudimentary vision maximally for blue light. A potential criticism that the responses could have been due to heat would be misplaced, as heat is dissipated at higher wavelengths and would cause the sensation of greatest response with long wavelength (yellow and red) light, and not with short wavelength blue light as the researchers found.

Chapter 21

Optic Chiasm

Brain: Optic chiasm	
	
Visual pathway with optic chiasm (X shape outlined, red) (1543 image from Andreas Vesalius' *Fabrica*)	
Latin	*chiasma opticum*
MeSH	*Optic+chiasm*
NeuroLex ID	*birnlex_1416*

The **optic chiasm** or **optic chiasma** is the part of the brain where the optic nerves (CN II) partially cross. The optic chiasm is located at the bottom of the brain immediately below the hypothalamus.

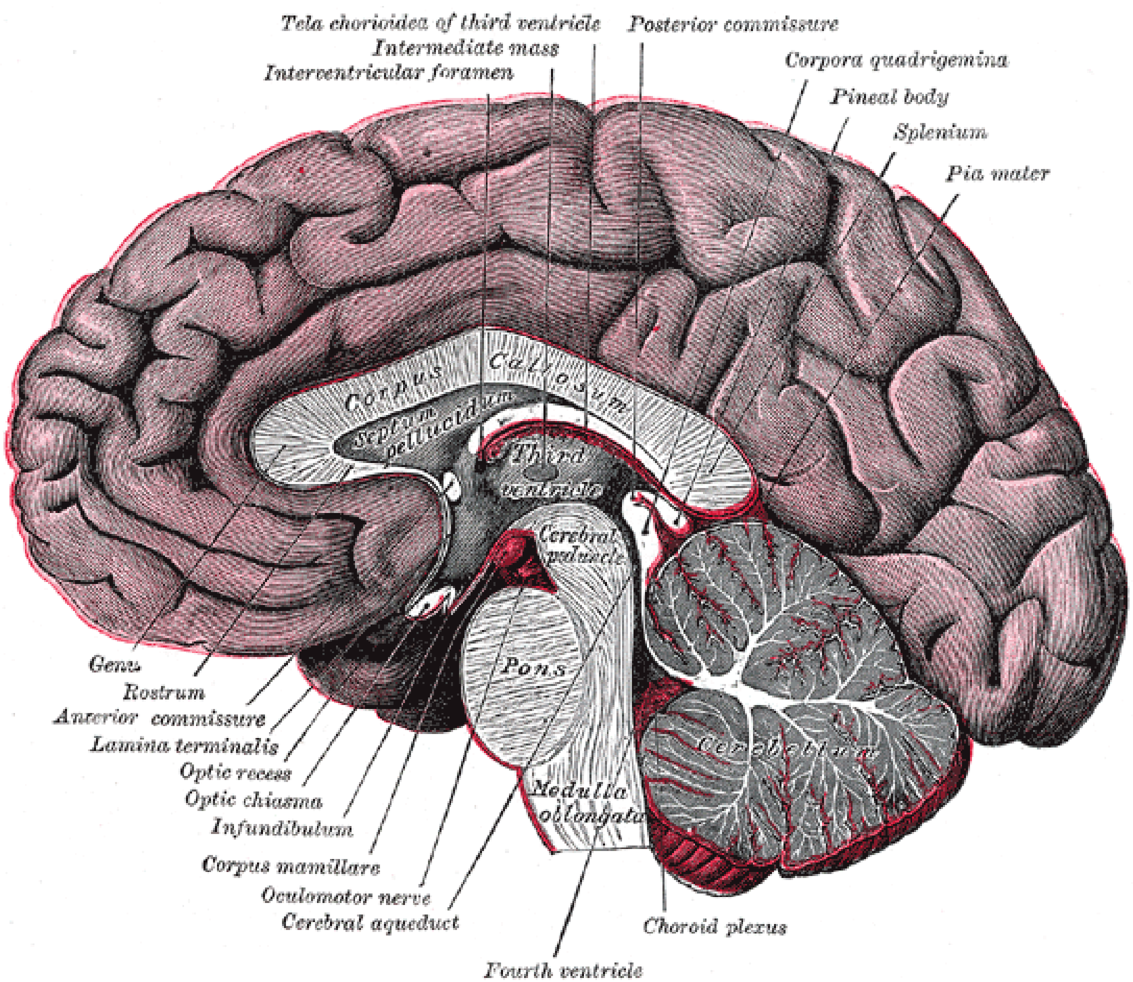
Pathways

The images on the nasal sides of each retina cross over to the opposite side of the brain via the optic nerve at the optic chiasm. The temporal images, on the other hand, stay on the same side. This allows the images from either side of the field from both eyes to be transmitted to the appropriate side of the brain, combining the sides together. Beyond the optic chiasm, with crossed and uncrossed fibers, optic nerves become optic tracts. This allows for parts of both eyes that attend to the right visual field to be processed in the left visual system in the brain, and vice versa. This is linked to skin sensation which reaches the opposite side of the body, after reaching the diencephalon (rear forebrain). Decussation is an adaptive feature of frontally oriented eyes and therefore having binocular vision. Some animals, with laterally positioned eyes, have little binocular vision, so there is a more complete crossover of visual signals. The signals are passed on to the lateral geniculate body, in turn giving them to the occipital cortex (the outer matter of the rear brain).

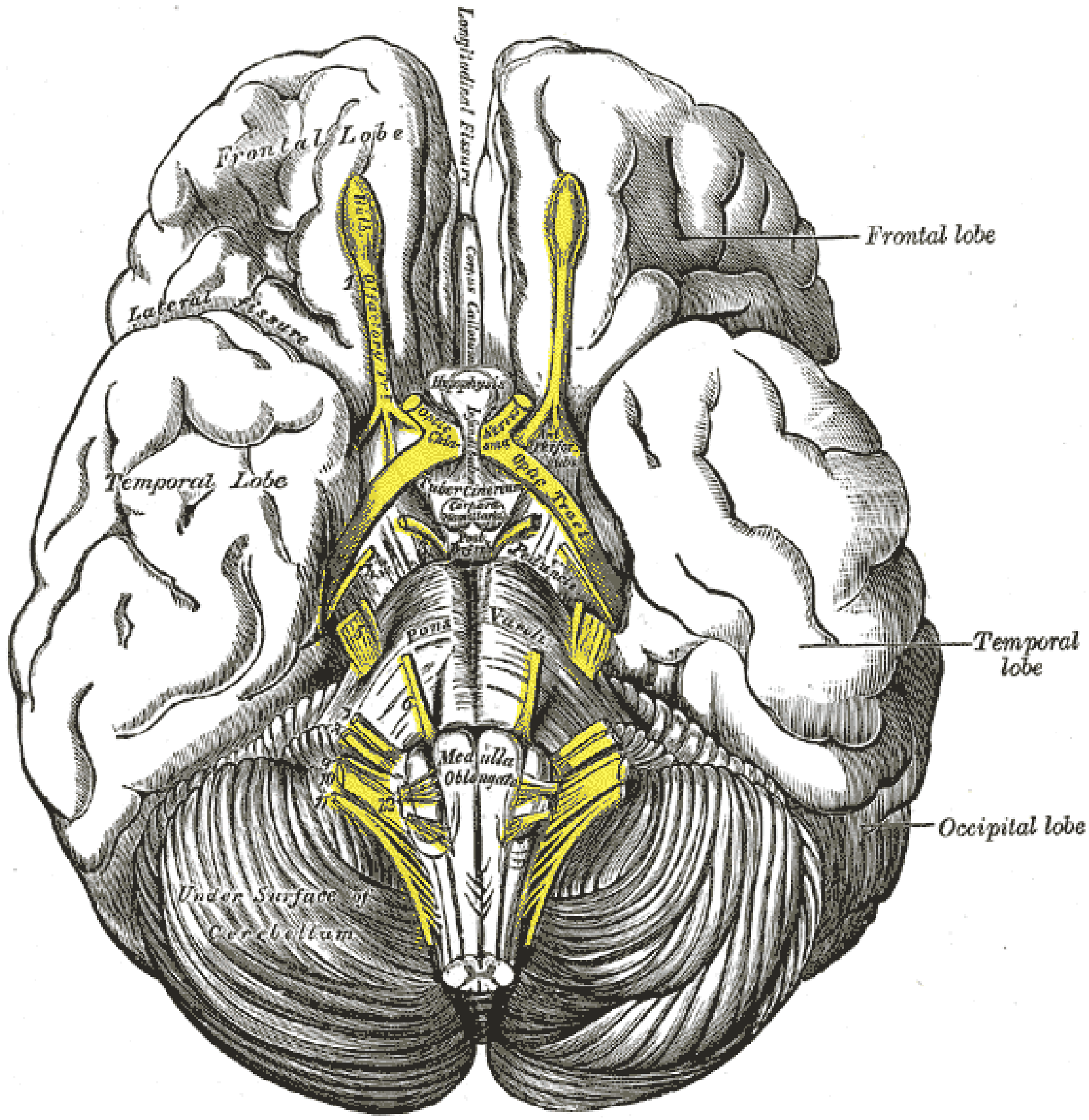
Optic chiasm in cats

In Siamese cats with certain genotypes of the albino gene, this wiring is disrupted, with less of the nerve-crossing than is normal, as a number of scholars have reported. To compensate for lack of crossing in their brains, they cross their eyes (strabismus).

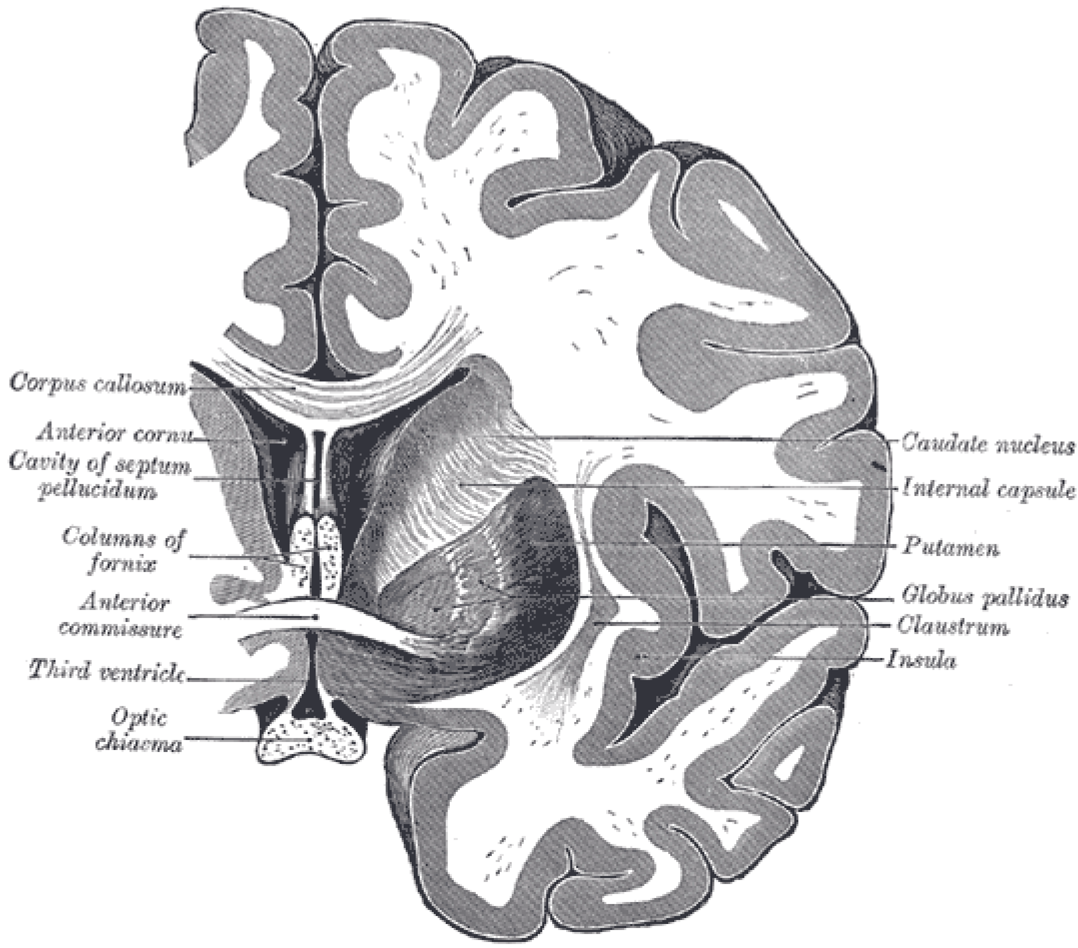
This is also seen in albino tigers, as Guillery & Kaas report.



Median sagittal section of brain



Base of brain



Coronal section of brain through anterior commissure

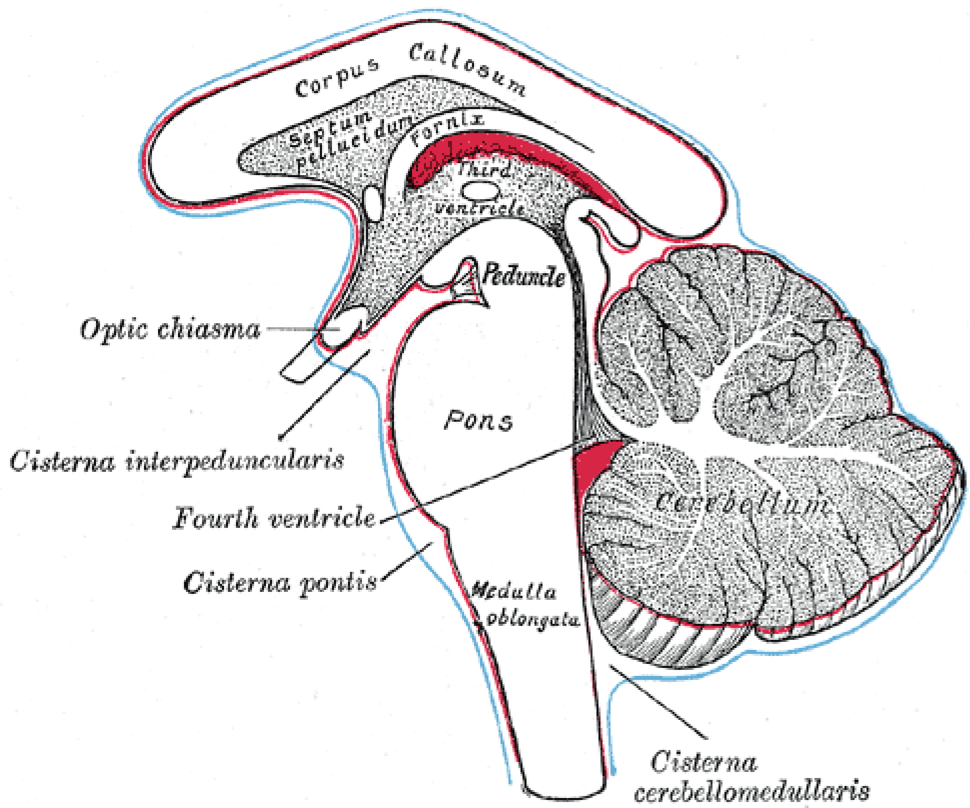
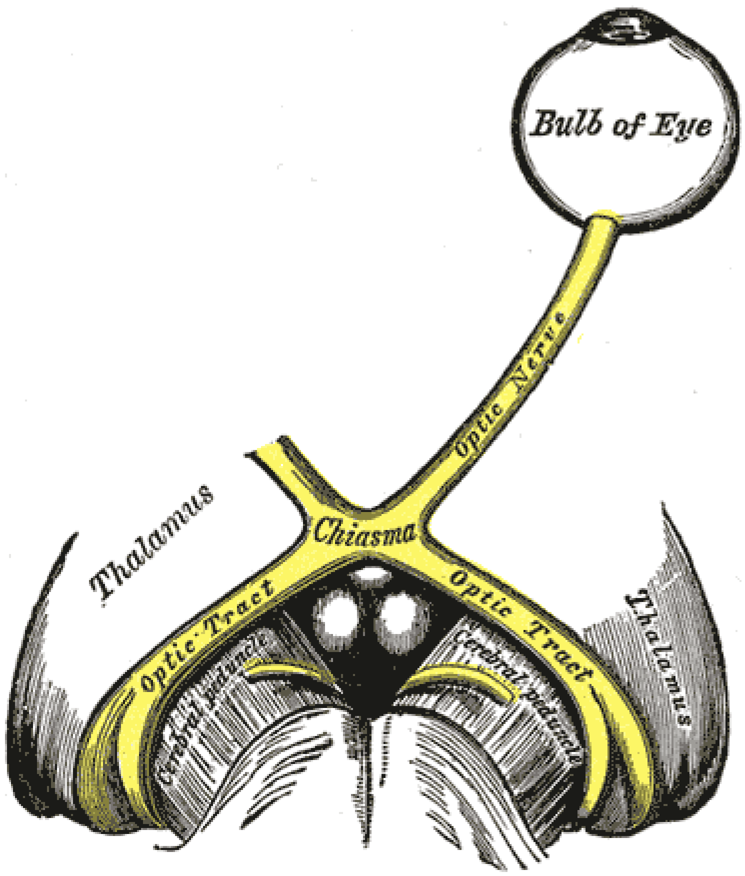
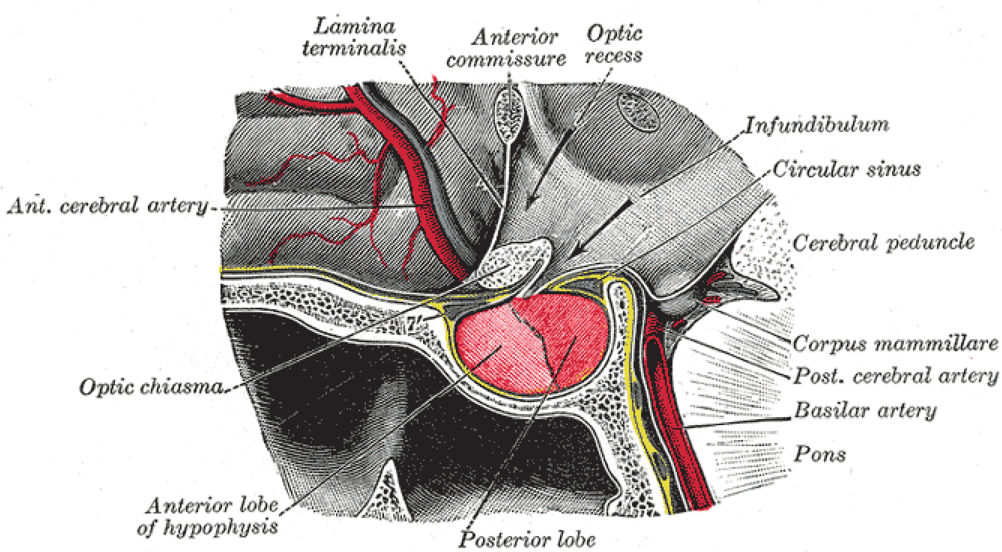


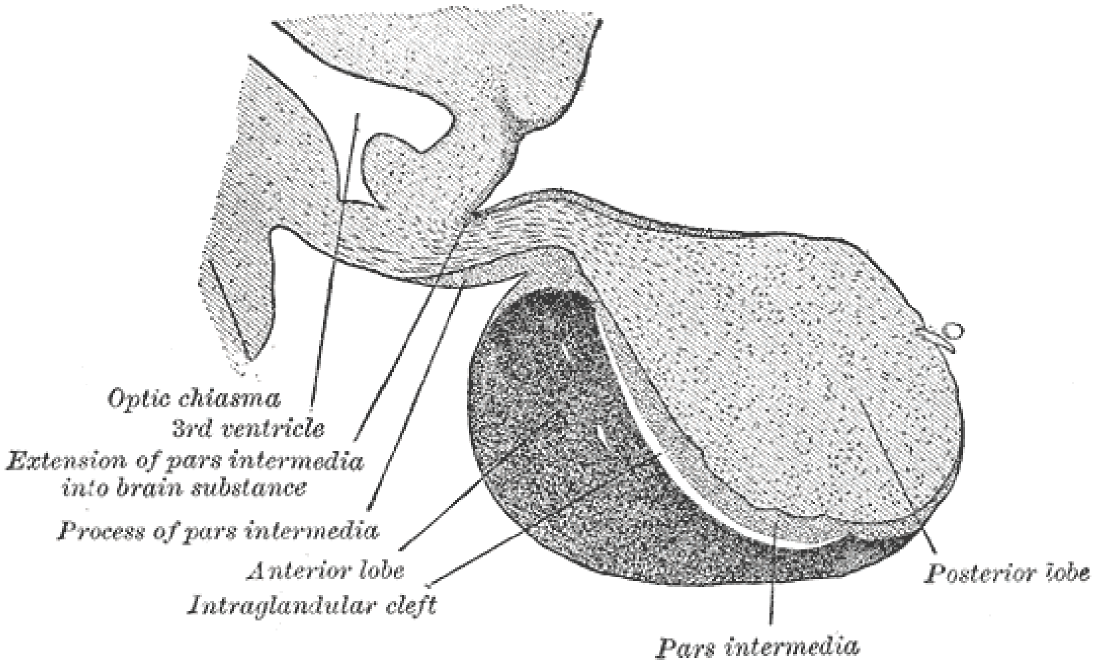
Diagram showing the positions of the three principal subarachnoid cisternæ



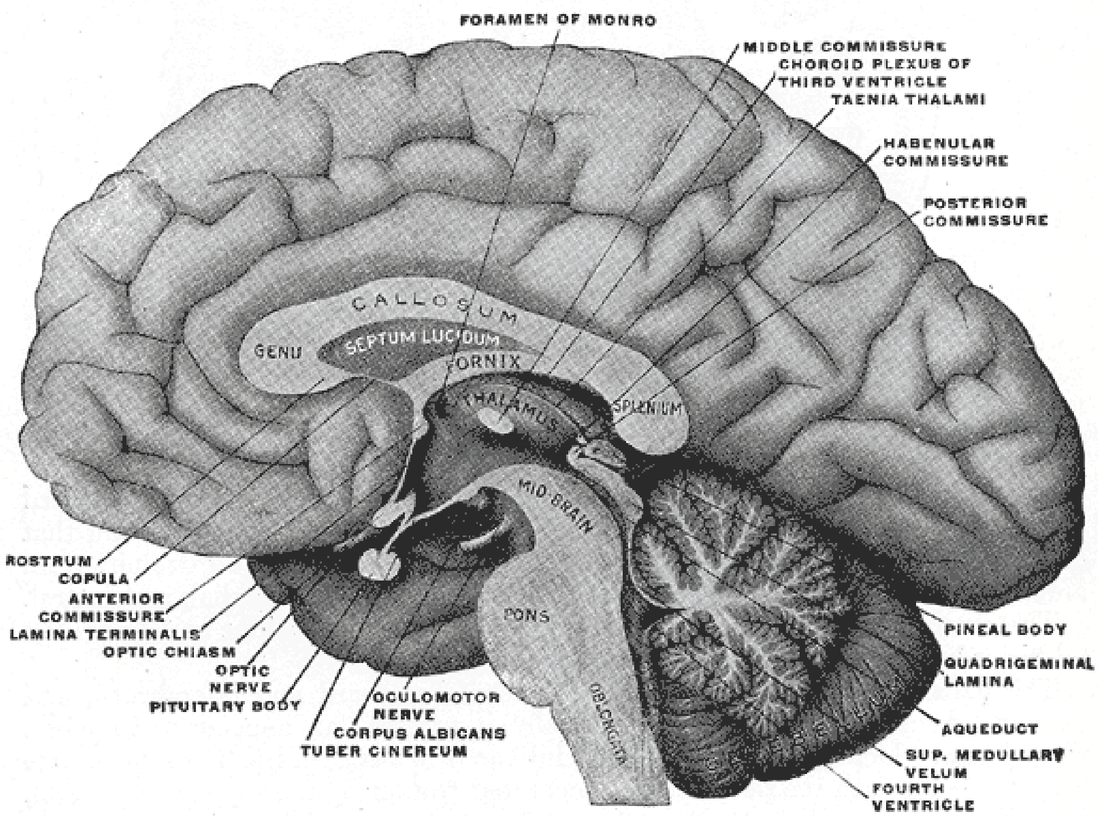
The left optic nerve and the optic tracts



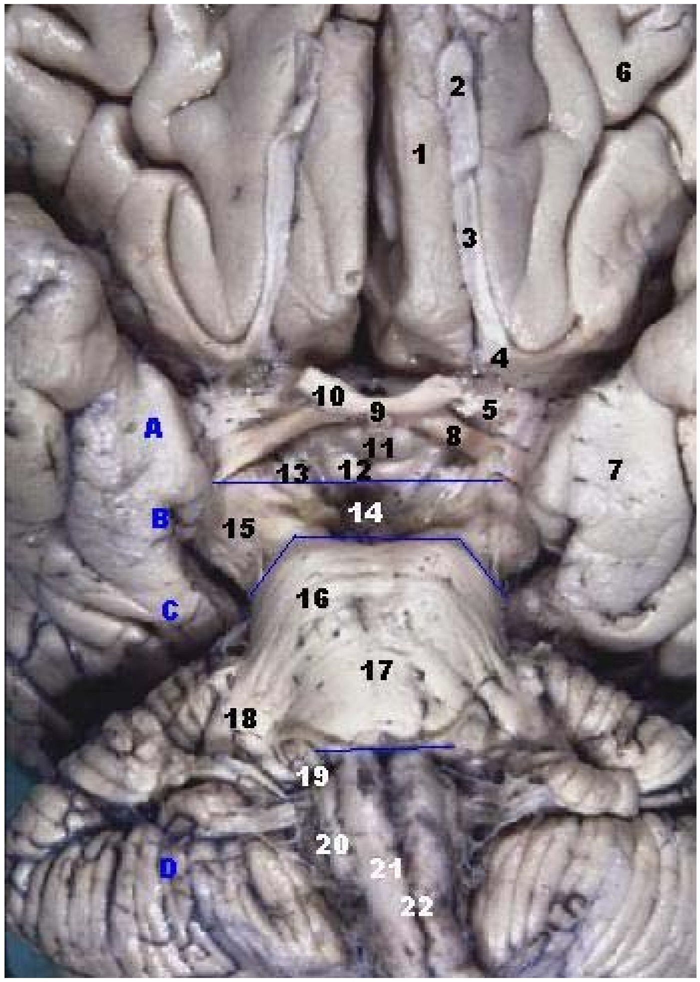
The hypophysis cerebri in position. Shown in sagittal section.



Median sagittal through the hypophysis of an adult monkey. Semidiagrammatic.



Mesal aspect of a brain sectioned in the median sagittal plane



Human brainstem anterior view