

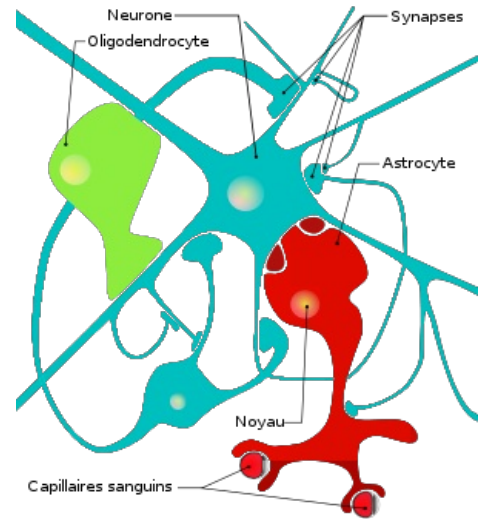
# Glial cells, brain barrier systems

## Glial cells

Glial cells are also known as neuroglia, meaning nerve "glue".

### Macroglia

1. **Astrocytes:** they have light cytoplasm, astrocytic filamentous bodies, numerous processes and they can form a glial "scar". Their functions are:
  1. to contribute to the extracellular potassium concentration maintenance
  2. to cover the basal lamina of the capillaries (part of the blood-brain-barrier) and transport some of the nutrients to neurons through their cytoplasm
  3. to cover the surface layer of the CNS (glia limitans)
  4. to cover the surface of neurons, fill in the interneuronal spaces
  5. by finger-like processes surround and isolate synaptic clefts, astrocytes may contribute to the inactivation of neurotransmitters (GABA, glutamate, glycine)
  6. after the brain is damaged, they form astrocytic scar (preventing the regrowth of central axons)
2. **Oligodendrocytes:** they contribute to the surface cover (myelination) of neuronal bodies and processes (glial cell processes surround unmyelinated fibers, layers of myelin). Oligodendrocyte's plasma membrane contains voltage-gated ion channels. Myelin-forming cell furnishes channels for the axon → myelin provides a signal to prevent the insertion of sodium channels into the internodal region of a myelinated nerve fibre.



Neuron glial cells diagram fr

### Microglia

Microglia are functionally similar to macrophages; is probably of mesodermal origin; microglial cells are activated by some pathologic and reparatory processes in the CNS (gliosis)

### Ependymal cells

They line the internal cavities of the CNS - part of the blood-brain barrier and they can absorb and secrete cerebrospinal fluid.

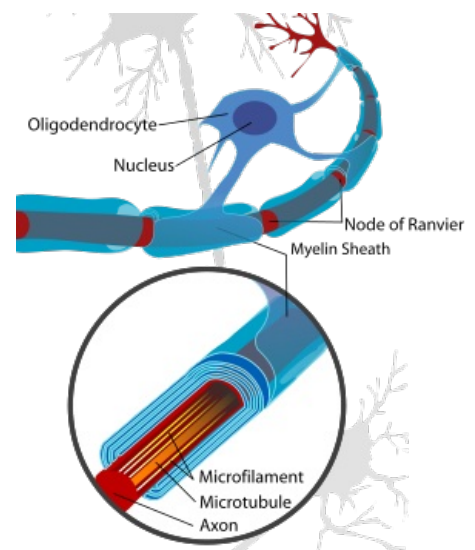
## Myelin Sheath

**Myelin sheath** is formed by oligodendrocytes in the CNS and by Schwann cells in the peripheral nervous system. These cells wrap layer upon layer of their own plasma membrane in a tight spiral around axon. Each myelinating Schwann cells makes myelin layers at a single axon, forming a segment (internodium) that is about 1 mm long and consisting of up to 300 concentric layers of membrane.

Between one segment of sheath and the next, small regions of axon membrane remain bare (node of Ranvier).

Oligodendrocytes form similar segments of sheath at many separate axons simultaneously.

The insulating layer of the myelin sheath reduces the effective capacitance of the axon membrane and prevents almost all current leakage across it. Practically all the  $\text{Na}^+$  channels of the axon are concentrated at the nodes, giving the density of several thousand channels per  $1 \text{ mm}^2$ . The sheathed portion of the axon membrane is not excitable, but has excellent cable properties. The membrane at the node of Ranvier is highly excitable and maintains the amplitude of the action potential → saltatory conduction, leading to acceleration of the conduction and conservation of the metabolic energy.



Neuron with oligodendrocyte and myelin sheath

The following GIF (<http://lecannabiculteur.free.fr/SITES/UNIV%20W.AUSTRALIA/mb140/CorePages/Nervous/Images/Myelinani.gif>) schematizes the process of myelination by a Schwann cell.

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## **Control of extracellular potassium concentration**

Glial cells have a resting potential of about -90 mV (more negative than a typical neuronal membrane), which is nearly identical to  $E_K$  (equilibrium potential for  $K^+$ ). Plasma membrane contains various densities of  $K^+$  channels, which are employed in the control of ECF's  $[K^+]$ , voltage-gated  $Na^+$ ,  $K^+$ ,  $Ca^{2+}$  channels, which incorporated into the neuronal membrane and/or may serve to generation of electrical signals with  $Ca^{2+}$  probably serving as a second messenger. Gap junctions among glia cells provide a low-resistance pathway for intercellular ionic current and a flow of some substances.

During the repolarization phase and the afterhyperpolarization of each neuronal action potential, a small amount of potassium leaves the neurons into the ECF. Following a sustained neuronal activity, a local increase in  $[K^+]$  can be detected. This increase must be cleared to prevent depolarization of neurons and synaptic terminals in the vicinity, through the following ways:

1. Diffusion (a comparatively slow process)
2. Flow of potassium current through glia (spatial buffering) - as the glial resting potential lies close to  $E_K$ , increase of extracellular  $[K^+]$  depolarizes the glial membrane:
  1. Since the depolarized cells are somewhat negative to the local  $E_K$ , potassium enters the cell and serve as charge carriers to the less depolarized regions of the glial syncytium
  2. the electrical circuit is completed by the extracellular flow of sodium and chloride ions →
  3. redistribution of  $K^+$  during the neuronal activity
3. Active transport of extracellular  $K^+$  back into neurons back the glia.

Glial cells at the site of an old brain injury are not as efficient in the spacial buffering of potassium ions → tendency for epileptic seizures in regions of an astrocytic scar, due to rise of ECF  $[K^+]$  → depolarization → increased excitability (e.g.: seizures)

## **Blood Brain Barrier**

There are 3 brain barrier systems:

1. Blood-peripheral nerves and ganglia barrier system
2. Blood-cerebrospinal fluid barrier
3. Blood-brain barrier (BBB)

Barriers are functionally immature in the human neonates - potential danger of bypassing by various toxic and pharmacological agents (bilirubin, PNC).

## **Locations without covering**

Some small CNS regions are out of the BBB:

1. Area postrema of the fourth ventricle
2. Subfornical organ
3. Epiphysis
4. Neurohypophysis
5. Median eminence

All the above structures have some common characteristics:

1. They are located on the midline ventricular surface
2. Majority of their capillaries are fenestrated
3. They are employed in neurosecretory function
4. They contain receptors for various blood-borne molecules (e.g., peptide hormones) - the ability to have full access to the blood content enables them to sense osmolarity, glucose concentration, etc, correctly

## **Permeability**

The low permeability is due to tight junctions (zonae occludens). For substances that need to access areas that are covered by the BBB, such as leptin, there are specific carrier proteins that enable transport of such hormones (bidirectionally), from the blood into the hypothalamus for example.

The layers of the BBB consist of:

1. the capillary endothelium, connected via tight junctions (zonulae occludens)
2. a continuous homogeneous basement membrane
3. the processes of numerous astroglia

The BBB is:

- High permeability for: water, carbon dioxide, oxygen, most lipid-soluble substances (e.g.: alcohol and anesthetics)
- Little permeability for: electrolytes (e.g.:  $\text{Na}^+$ ,  $\text{Cl}^-$ ,  $\text{K}^+$ )
- Almost totally impermeable to: plasma proteins and most non-lipid-soluble large organic molecules.

It is obvious that the blood-cerebrospinal fluid and blood-brain barriers limit the degree of how much drug can enter the cerebrospinal fluid or parenchyma of the brain. Such drugs may be protein antibodies and other non-lipid-soluble drugs.

## Transport of nutrients

- Electrolytes: the basal surface membrane of capillary endothelial cells contains  $\text{Na}^+/\text{K}^+$  ATPase, which removes  $\text{Na}^+$  from the cell into the brain extracellular fluid. Electroneutrality is maintained by transport of  $\text{Cl}^-$  ( $\text{Cl}^-$ -bicarbonate antiport, bicarbonate is formed within the epithelial cells).
- Glucose: glucose combines with a carrier protein on the luminal surface of the endothelial cell and is transported across the cell membrane. The carrier then dissociates and it is recycled. Glucose transport across brain capillary endothelia is not coupled with sodium and it is not dependent on insulin (similar to that in the red cell membrane - GLUT1 transporter).
- Amino acids: amino acids are transported by similar facilitated transport mechanisms (three different systems for neutral, acidic, and basic amino acids).

## Functions of the BBB

1. Protection of the nervous system from pathogens
2. Precise local environment regulation
3. Retaining of certain factors within the brain (neurotransmitters, neuromodulators)

## Links

### Related articles

### Sources

- Lecture Notes: Prof. MUDr. Jaroslav Pokorný DrSc.

### Bibliography

- HALL, John E – GUYTON, Arthur Clifton. *Guyton and Hall Textbook of Medical Physiology*. 11. edition. Saunders/Elsevier, 2005. ISBN 0721602401.
- DESPOPOULOS, Agamnenon – SILBERNAGL, Stefan. *Color Atlas of Physiology*. 5. edition. Thieme, 2003. ISBN 3135450058.

### Further reading