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.: Na^+, Cl^-, 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 Na^+/K^+ ATPase, which removes Na^+ from the cell into the brain extracellular fluid. Electroneutrality is maintained by transport of Cl^- (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

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Further reading