Milieu of Central Nervous System

In order the brain functions proceed efficiently, neurons have to be kept in a proper and constant environment (=milieu). This environment provides the following:

1. protection from damage
2. insulation from unwanted electrical signals
3. guarantee of an appropriate ionic milieu
4. provision of energy and building substrates

Cerebrospinal Fluid (CSF)

The cerebrospinal fluid as a hydraulic shock absorber. The subarachnoid space, between the arachnoid and pia, contains the CSF, in which the brain and the spinal cord are suspended. The displayed CSF reduces the effective weight of the brain (1400-1500g in the air) to less than 50g, thus decreasing the danger of brain damage during sudden acceleration of the head. The CSF also fills the ventricular system (lateral ventricles, third ventricle, four ventricle - communications to subarachnoid space (subarachnoid cisterns), central canal in the spinal cord), thus enabling possible changes in volume of individual spaces for compensating possible volume changes of the brain (due to change in intensity of blood flow or atrophy).

Secretion & Composition of CSF

About two thirds of CSF is secreted from the choroid plexus, one third diffuses from the extracellular fluid in the nervous tissues and from the ependymal cells. The flow of CSF is accelerated by the activity of ependymal cilia. The volume of the CSF is about 140 ml (adult human), about 500 ml of CSF is formed daily. The pressure in the CSF column is about 120 to 180 mm H_2O.

The CSF has the same constituents as the blood plasma, but:

- lower concentration of K^+ (-40%)
- lower glucose (-30%)
- lower protein
- larger concentration of Cl^- (+15%);

It contains no blood cells, and is isotonic to blood.

The blood flow through the choroid plexus is larger than the blood flow through the kidney. The components of CSF, that originate in the blood must pass through (first→last):

1. the capillary endothelium (fenestrated)
2. the surrounding extracellular matrix (loose)
3. the single layer of choroid plexus epithelial cells (regulation of the fluid and ion movement)

The choroid cells secrete CSF by the transcellular transport of sodium, chloride and bicarbonate ions. The apical brush border contains Na^+/K^+ ATPase pumps. To preserve electroneutrality, chloride and bicarbonate accompany the transport of Na^+ (Na-Cl cotransport, bicarbonate-Cl antiport). Water (follows by osmosis) and some small molecules can pass between epithelial cells across the tight junctions.

The choroid plexus receives both a cholinergic and adrenergic innervation.

Absorption of the CSF

Absorption is carried out by the arachnoid granulations. These structures protrude into the sagittal venous sinus. Their cells are attached to each other by tight junctions and contain large vesicles. Majority of the flow transport across cells of the arachnoid granulations is by the sequential pinocytosis and exocytosis of large vacuoles. Little CSF absorption occurs until the CSF pressure exceeds 70 mmH_2O.

Nutrient supply to the brain

Only pial and ependymal surfaces of the brain receive some nutrients from the CSF. Deeper structures are supplied from the blood circulation. The capillary endothelium, a continuous homogeneous basement membrane, and the processes of numerous astroglia separate the plasma from the extracellular space of the CNS form an effective barrier that permits only selected substances to pass (blood-brain barrier - BBB). The BBB allows passage of small nutrients and water and remove of waste products. It prevents movements of large molecules and specifically active molecules. The major barrier is the tight intercellular circumferential junctions (zonula occludens) joining the endothelial cells of the brain capillaries. Transport by pinocytosis seems to be also very limited. Paracellular transport of water and small molecules can occur (its increase becomes an important mechanism of the brain swelling).

- 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).

Extracellular space

Though EM pictures show almost no extracellular space, physiological studies using radioactive tracers show that the extracellular space constitutes 15 to 20% of the brain tissue. To keep the electrical properties of neurons, the concentration of the extracellular fluid constituents in the brain is closely maintained (e.g., fluctuation in $[K^+]$ may affect the resting potential level and/or synaptic transmission). The ECF allows nutrients, wastes and message chemicals to move within the CNS. Though its limited size and tortuosity and the presence of an extracellular glycoprotein matrix, it itself does not present a significant barrier to the movements of these molecules.

Circumventricular organs

These organs have limited BBB covering and they are located at the margins of the ventricular system of the brain.

Circumventricular organs (CVOs) include:

1. Median eminence
2. Neurohypophysis
3. Area postrema
4. Organum vasculorum lamina terminalis
5. Subfornical organ
6. Subcommissural organ and the pineal gland

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)

Possible functions of the CVOs

1. Receptor site for circulating angiotensin II: mediation of its central effect (increase in water intake, increase of blood pressure; increase in ADH release)
2. High binding activity for estrogen hormones - location of one of the feedback mechanism for cyclic gonadotropin secretion control
3. Chemoreceptive trigger zone (especially at area postrema): a site at which the transduction of the signal of blood-borne chemical substances to various autonomic reactions (e.g., various toxins → vomiting reflex - taste aversion learning, cancer anorexia; nutritional products and gastrointestinal peptides → control of food intake, metabolism).

Links

Related articles

- Glial Cell
- Blood Brain Barrier

Sources

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

Bibliography

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Further reading