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Review Article

The Study of Neuroglia Under an Electron Microscope

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Abstract

With the help of a light microscope, you can see several types of cells: neuroglia lying next to neurons and their processes. Neuroglia of ectodermal origin consists of oligodendroglia, fibrous and protoplasmic astrocytes and cubic ependymal cells with cilia. The latter line the ventricles and the central canal of the brain and spinal cord. The smallest of the glial cells forming microglia are of mesodermal origin and can turn into phagocytes. Various types of glial cells are usually recognized using various staining methods. For example, on preparations stained by Nissl, it can be seen that astrocytes have the largest nuclei, usually oval in shape and most often with fine-grained, evenly distributed chromatin. Oligodendroglia cells have smaller rounded nuclei with dense lumps of chromatin, especially crowded at the nuclear envelope. The nuclei of microglial cells are smaller and more often elongated. Special methods of silvering reveal bundles of glial fibrils in the long undulating processes of fibrous astrocytes; in microglial cells, the cytoplasm is usually stained entirely; their several processes are characterized by branching at an "angle". In oligodendroglia cells, the nuclei are rounded: these are cells with a small number of short processes (as indicated by their name) or without any processes at all. Astrocytes, which are best seen when colored by Golgi, have numerous branching, feathery processes. These are the main features, but there are many differences, and since it is often impossible to reliably recognize all types of cells using light microscopy on a single slice of brain tissue, it is not surprising that even with electron microscopic examination, cells that are difficult to classify are often found. Nevertheless, a number of criteria have been established that can be used, however, with caution.

Key words: neuroglia; electron microscope; methods

Introduction

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1.Cell types

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a. Oligodendroglia. Cells of this type are involved in the formation and maintenance of myelin sheaths. They are easily recognized in the white matter of the brain using light and electron microscopy, as they lie in chains between bundles of myelin fibers. Chunks of chromatin are clearly visible in their nuclei, and the narrow rim of the cytoplasm contains a large amount of granular endoplasmic reticulum and many mitochondria. Cells with similar signs are found throughout the gray matter, where there are, of course, myelin fibers. It is often possible to see a myelinated axon (in this case in the

cerebral cortex) lying inside the groove of the cytoplasm. And yet, despite the prevalence of such a picture, it has not yet been possible to trace a continuous connection between the cytoplasm of the oligodendroglia cell and myelin plates in the tissue of an adult organism. This could mean that only a narrow "neck" of the oligodendrogliocyte cytoplasm fits to the axon, which then expands and flattens to form myelin plates. Then we would have only a very small chance to make a cut through this narrow neck in such a plane as to simultaneously see both the myelin sheath and its continuous connection with the glial cell. [5]

Satellite cells, which are constantly found in association with larger neurons, usually belong to the oligodendroglia, and with the help of an electron microscope, it is often possible to identify cells that occupy a typical satellite position and have signs of oligodendroglia cells. Occasionally, however, we also had to see small rounded satellite cells with a narrow rim of relatively light, non-granular cytoplasm. Such cells are difficult to classify without knowing what their size and three-dimensional structure are. [6]

b. Astrocytes. It is usually believed that these cells have a pale, "watery" cytoplasm, which practically does not contain a granular endoplasmic reticulum and relatively few mitochondria. They form a boundary layer of cell bodies under the soft meninges and a layer of "terminal legs" around blood vessels. Apparently, there are no clear differences in fine structure between protoplasmic and fibrous astrocytes, except for the fact that the cytoplasm of fibrous astrocytes may contain numerous bundles of fibrils. [7]

The outer basement membrane separates this layer from the soft meninges, which are mostly removed in this preparation. The astrocyte contains an underdeveloped granular reticulum and a Golgi apparatus. This is undoubtedly a fibrous astrocyte, since a compact bundle of fibrils is visible in it, going from a lateral process through the cell body to another process that descends into the depths of the substance of the cortex. A very similar picture can be seen in a light microscope when examining fibrous astrocytes impregnated with silver. [8]

Astrocytes are usually credited with an important role in the metabolism between neurons and the circulatory system. Some authors also believe that the extraneuronal sodium space, which is important for the formation of the membrane potential, is not exhausted by the intercellular gap with a width of 200 A, but also includes the cytoplasm of astrocytes. The role of astrocytes in the blood-brain barrier has already been mentioned.

Fibrils are particularly well developed in mammalian spinal cord astrocytes. They seem to consist of protein, so it is interesting to note the immediately striking absence of a granular reticulum in astrocytes, which is usually considered responsible for protein synthesis.[9]

c. Microglia. The fine structure of these cells is much less understood. It has been described that microglia elements as cells with extremely high density. One such cell from the cerebral cortex of a rat is shown in photo 242. Its cytoplasm contains tightly packed granules, so that the channels of the endoplasmic reticulum appear very pale against this background. The nucleus is dense and strongly bumpy — it is only difficult to distinguish the boundary between it and the surrounding cytoplasm. Neurons that have darkened and shrunk due to poor fixation or mechanical compression sometimes acquire approximately the same appearance. [10]

d. Ependyma. These cubical cells covered with cilia form a lining (often single-layered in mature animals) of the ventricles and the central canal of the brain and spinal cord. Their basal processes are usually in direct contact with the processes of neurons and glial cells in the gray and white matter of the brain — there is no basement membrane between them. The nucleus is located in the basal region, and the Golgi apparatus and the granular reticulum are located at the apical pole. Some of the cells contain coarse bundles of filaments. A small number of ependymal cells have elongated basal processes, and other cells have branched processes. These are, respectively, Horstmann's tanicytes and ependymal astrocytes. [11]

2. Extracellular spaces and the relationship between glial elements and vessels

So far, no extensive extracellular channels have been detected in the gray and white matter of the mammalian central nervous system using electron microscopy. The light zones between the cell processes in the fixed material have a width of about 200— 400 A. We know little about the structure of these light intercellular spaces, their role in the diffusion of ions and metabolites, and about the chemical and physical forces acting in such narrow gaps. It is especially important to study the role of these slits in diffusion, since the processes of neurons in most parts of the brain are not in direct contact with the walls of blood vessels or cerebrospinal fluid of the ventricles, central canal and subarachnoid space. The metabolism between these components, as a rule, is carried out indirectly, and these pathways are directly related to the so-called blood-brain barrier, the idea of which originally arose as a physiological concept. [12]

Currently, it is extremely difficult to give a clear definition of what is meant by the "hemato-encephalic barrier". Many of the published data cited to prove the existence of specific "barrier phenomena" turned out to be characteristic not only of the brain, but also of other organs of the body in general. Nevertheless, many substances quickly pass from the blood to the brain and back, while others are unable to do this. In addition, there are certain structures in the brain, for example, a gray hillock, supraoptic, subfornical and postremal areas, neurohypophysis and epiphysis, where the metabolism of substances (for example, dyes, labeled phosphorus or bromine and large protein molecules) is fast, but in other areas of the brain this is not observed [13]. Obviously, we can say that the hemato-encephalic barrier in these six brain structures does not function, and therefore any structures that are absent here, but are present in other parts of the brain, should be of particular interest for study. In addition, it is important to establish which structures are present in those parts of the brain where the barrier functions, but are absent in similar areas of tissues that are not related to the nervous system. In an adult organism, in those parts of the brain where the barrier functions, there is never direct contact of nerve elements with the basement membrane of capillaries. In the interval there are always neuroglia cells or, more often, their appendages in the form of terminal legs (see section OSH, K,1). Sometimes these layers are extremely thin on the order of 150-200 A, and they can be clearly seen only at high magnification in well-fixed tissues. Most of these cells are protoplasmic or fibrous astrocytes. [14]

Adjacent membranes of adjacent end legs form a specialized structure called a sealed contact. Such areas are shown in photo 244, the intercellular gap is narrowed here to 150 A, unlike the usual width of extracellular zones of 200 A (for example, x). In photo 243 (framed), these areas are presented at very high magnification (osmium-fixed material at the top, permanganate fixation at the bottom). Both sealed contacts have a five-layer structure and resemble terminal jumpers. The middle dense line probably corresponds to the adjacent outer surfaces of the converging glial cells, so that there is no discernible extracellular zone in this area. Thus, these sites serve as barriers blocking the pathways of extracellular diffusion. They are also places of special adhesion, since the membranes in these areas cannot be separated by immersion in sucrose solution or mechanical damage, unlike those areas where there is a gap 200 A wide. Similar barriers to diffusion exist between adjacent endothelial cells. [15]

The three-dimensional organization of diffusion barriers between the glial terminal legs is currently unknown, but it seems likely that these barriers prevent extracellular diffusion, ensuring intracellular passage through the cytoplasm of the glial cell of all material coming from the blood into the brain tissue.

Thus, the substances brought by the blood must pass, firstly, through the cytoplasm of the endothelium. This barrier is probably no different from the barrier of endothelial cells in general. Firstly, they need to pass through the basement membrane, but this membrane most likely does not serve as an obstacle to diffusion. In fact, it is a permanent part of all capillaries and is

found in many organs and tissues where rapid diffusion takes place. For example, it divides the synaptic cleft of the motor end plates, completely surrounds muscle fibers of various types and separates the vascular-free epidermis from the dermis. The basement membrane undoubtedly manifested itself as a kind of barrier for silver particles, but silver deposition was observed not only in the nervous tissue; it probably reflects the argyrophilic rather than barrier properties of the basement membranes. Thirdly, substances must pass through the glial layer with its compacted contacts, and, finally, through the surface membranes of the neurons themselves. Probably, the last two structures are the most significant components in the morphological basis of the hemato-encephalic barrier.[16]

Undoubtedly, in most organs equipped with vessels, parenchymal cells are in direct contact with the basal membranes of capillaries and there is no intermediate layer similar to the glial cytoplasm layer. Large "watery" astrocytes probably play an important role in the rapid intracellular transfer of metabolites to and from neurons, but at the same time ensure the selective nature of this transfer. [17]

The six brain structures that we cited as examples of areas where the barrier is modified or absent have not yet been studied in detail using a high-resolution electron microscope. However, an important observation was made — it was established that in the mammalian neurohypophysis and in the preoptic region of the silver carp, the bodies of neurons are directly adjacent to the basal membranes of capillaries and are not separated from them by a layer of neuroglia. Similar relationships between the processes of neurons and capillaries exist in the epiphysis. [18]

In addition to the hemato-encephalic barrier, it is possible to demonstrate the presence of physiological barriers between blood and cerebrospinal fluid (in the vascular plexus and subarachnoid spaces where these fluids are in close relationship with each other) and between cerebrospinal fluid and the brain, separated by the ependyma. [19, 21, 22]

Electron microscopy shows that the glial layer around the blood vessels passes without interruption into the soft meninges and is located under it. Astrocytes lying directly under the soft shell also form compacted contacts with each other, similar to those existing at the walls of blood vessels. Ependymal cells also form compacted contacts between each other, which may create a barrier similar to the barrier formed by the circumvascular terminal legs of astrocytes. Similarly, in the vascular plexus, the ependymal layer separates the cerebrospinal fluid from the capillaries, which in this case are surrounded by extensive extracellular spaces containing collagen fibers. [20]

Conclusion. Thus, the study of neuroglia under an electron microscope provides a fundamental basis for further research in the field of neuromorphology and provides prerequisites for the clinical study of the brain in normal and pathological conditions.

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