Middle East Research Journal of Medical Sciences
ISSN: 2789-7699 (Print) & ISSN: 2958-2024 (Online)
Frequency: Bi-Monthly
DOI: https://doi.org/10.36348/merjms.2024.v04i05.005

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Study of the Characteristics and Functions Astrocytes of the Nervous System

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Abstract: Astrocytes are glial cells located in the central nervous system, that is, in the brain and spinal cord. Like the rest of the glia, astrocytes play supporting roles concerning neurons, the main cells of the nervous system from a functional point of view. Astrocytes are formed from cells of the ectoderm, the layer of the embryonic disc from which the nervous system and epidermis arise, during the organism's early development. Like most glia, astrocytes start from undifferentiated cells similar to those that give rise to neurons. This article aims to relate the characteristics and functions of astrocytes in the brain nutrition function, in the memory and learning process of stroke. Concerned with outlining a public profile of quality research in the area, we sought to answer these questions based on a literature review in the main journals in the area (national and international) classified by the Coordination for the Improvement of Higher Education Personnel (CAPES). To complement this analysis with other types of documents such as books, scientific journals, documents, and digital platforms, the following analysis steps were followed: (1) exhaustive reading of each article aiming at a global understanding and discovery of the approach used by its authors; (2) identification of the central ideas of each article; (3) classification of the ideas around core meanings; (4) comparison between the different core meanings present in the articles studied; (5) classification of the core meanings into broader axes (themes) around which the authors' discussions revolved; and (6) writing of interpretative summaries of each theme. After analyzing the content of the articles, we sought to establish a dialogue between the themes found and the literature that served as a basis for introducing the present study.

Keywords: Brain, Glial cells, Neurogenesis, Neuronal Development, Synaptic Communication.

Review Paper

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How to cite this paper:
Marco Vinícios de Oliveira Santana *et al* (2024). Study of the Characteristics and Functions Astrocytes of the Nervous System. *Middle East Res J. Med. Sci*, *4*(5): 135-148.

Article History:
| Submit: 22.09.2024 |
| Accepted: 21.10.2024 |
| Published: 25.10.2024 |

1. INTRODUCTION

Anatomically, the nervous system is divided into the CNS (Central Nervous System), formed by the brain and spinal cord, and the peripheral nervous system (PNS), formed by nerves and nerve ganglia. In the CNS, there is a separation between the cell bodies of neurons and their extensions. The nervous system is the main regulator of our functions, exercising control over almost all activities or events at any given moment in our body. This control is achieved through the transmission of impulses that travel through the various neuronal circuits and the release of chemical mediators through the numerous terminals found in the cells (UNESP, 2020; Cabral-Costa, 2023; FAPESP, 2023; Health Direct, 2023; Abbott, 2024; Maestrovirtuale, 2024; UNIFAL, 2024).

Nervous tissue is sensitive to various stimuli from outside or inside the organism. When stimulated, this tissue can conduct nerve impulses quickly and, sometimes, over relatively long distances. It is one of the most specialized tissues in the animal organism. Nervous tissue has two main components: neurons, cells generally with long extensions; and various glial cells or neuroglia, which support neurons and participate in other important functions. A third component is the extracellular matrix, although it is extremely scarce in this tissue. The cells of the nervous system are divided into: The neurons which are responsible for receptive functions, and glial cells or neuroglia which are accountable for supporting and protecting (Liborio Neto, 2017; Queensland Brain Institute, 2017; Pinto-Duarte *et al.*, 2019; Salk News, 2019; UNESP, 2020; Cabral-Costa, 2023; FAPESP, 2023; Ken Hub, 2023; Abbott, 2024).

Neurons are the cells responsible for receiving and transmitting stimuli from the environment (internal and external), enabling the organism to execute appropriate responses to maintain homeostasis. To

perform these functions, they rely on two fundamental properties: excitability and conductivity. Excitability is the ability that allows a cell to respond to stimuli, whether internal or external. Therefore, excitability is not a response, but the property that makes the cell capable of responding. This property is inherent to the various cell types in the organism (Figure 1) (Queensland Brain Institute, 2017; UNESP, 2020; Cabral-Costa, 2023; FAPESP, 2023; Abbott, 2024; Maestrovirtuale, 2024; Mental Health America-MHA, 2024; UNIFAL, 2024).

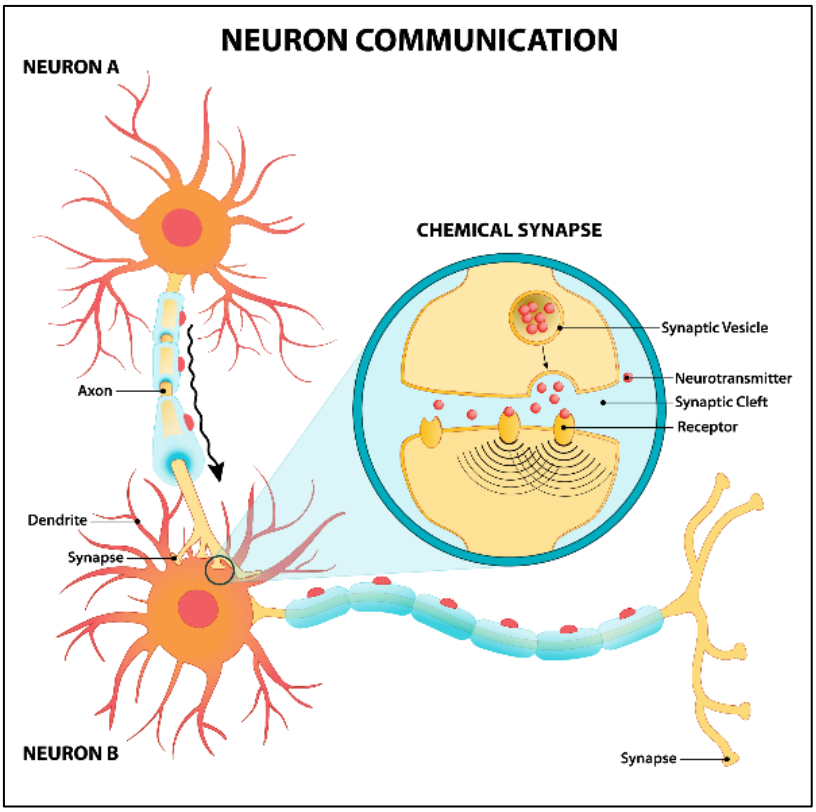

Figure 1: The junction where two neurons meet is called a synapse and is where intercell communication takes place. Neurons communicate with one another through action potentials (changes in a neuron's electric potential) and neurotransmitters

Source: https://mhanational.org/neurons-how-brain-communicates

Neurons comprise the cell body or perikaryon, dendrites, and axons. Perikaryon or cell body: This is the structure where protein synthesis occurs, and it is also here that the electrical currents generated in the dendritic tree converge. Each neuronal cell body contains only one nucleus located in the center of the cell. This structure also generally houses all cellular functions (Lima, 2009; Liborio Neto, 2017; Ken Hub, 2023; Maestrovirtuale, 2024).

Glial cells have the function of surrounding and nourishing neurons, keeping them together. The main types of cells of this nature are astrocytes, oligodendrocytes, microglia, and Schwann cells. Thus, glial cells act as support cells for neurons. Among the various functions performed by these cells, we can highlight the support and isolation of neurons; Transport of nutrients to neurons; Participation in the ionic balance of the extracellular fluid; Removal of waste, and phagocytosis of cellular debris (Liborio Neto, 2017; Pinto-Duarte *et al.*, 2019; Cabral-Costa, 2023; FAPESP, 2023; Ken Hub, 2023).

1.1. Glial cells

1.1.1. Astrocytes: They have numerous extensions; in large quantities. Their functions are support, and they participate in the ionic and molecular composition of the extracellular environment of neurons. Some astrocytes have extensions called vascular feet, which expand over the blood capillaries; these extensions transfer molecules and ions from the blood to the neurons.

1.1.2. Oligodendrocytes: Produce myelin sheaths that serve as electrical insulation for neurons in the central nervous system (CNS). Oligodendrocytes have extensions that wrap around axons, producing the myelin sheath.

1.1.3. Microglia: These are small cells with some extensions, present in both white matter and gray matter. They are phagocytic cells and derive from precursors brought from the bone marrow by the blood, representing the mononuclear phagocytic system in the central nervous system.

1.1.4. Schwann cells: They have the same function as oligodendrocytes but are located around the peripheral nervous system. Each Schwann cell forms a myelin sheath around a segment of a single axon and has extensions that wrap around several axons. This myelin sheath acts as an electrical insulator and contributes to increasing the speed of propagation of the nerve impulse along the axon. Between one Schwann cell and another, there is a region of discontinuity in the sheath, called the node of Ranvier.

1.1.5. Ependymal cells: Ependymocytes are columnar or cuboidal epithelial cells that line the ventricles and central canal of the spinal cord. As such, they are essential for the movement of cerebrospinal fluid, or CSF, throughout the CNS.

1.1.6. Satellite cells: The cells are mononuclear progenitor cells found in mature muscle between the basal lamina and the sarcolemma. These cells are capable of differentiating and fusing to increase the number of existing muscle fibers and to form new fibers (Figure 2) (Pinto-Duarte *et al.*, 2019; UNESP, 2020; Cabral-Costa, 2023; FAPESP, 2023; Ken Hub, 2023; Abbott, 2024).

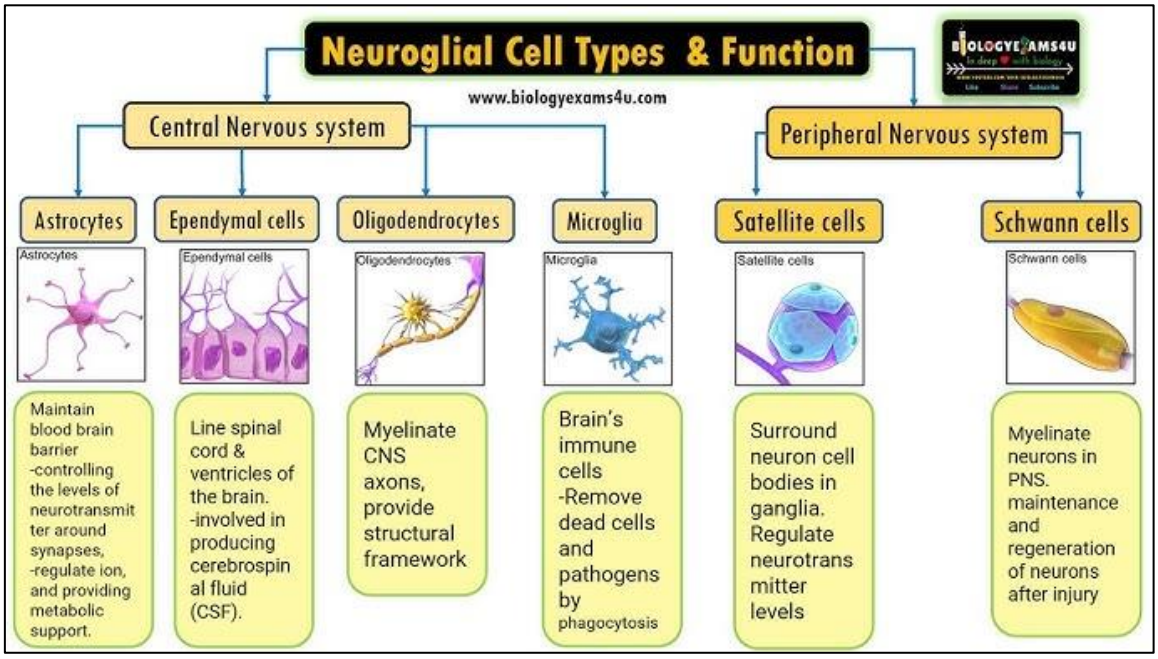

Figure 2: Neuroglial cell types by location and basic function 6 types of glial cells and their function
Source: https://www.youtube.com/watch?app=desktop&v=-k5cDbFxGl0

1.2. Astrocytes

Astrocytes are glial cells located in the central nervous system, that is, in the brain and spinal cord. Like the rest of the glia, astrocytes play supporting roles concerning neurons, the main cells of the nervous system from a functional point of view. Astrocytes are formed from cells of the ectoderm, the layer of the embryonic disc from which the nervous system and epidermis arise, during the organism's early development. Like most glia, astrocytes start from undifferentiated cells similar to those that give rise to neurons (Ken Hub, 2023; Abbott, 2024; Maestrovirtuale, 2024; UNIFAL, 2024).

1.3. Functions

1. Contribute to the formation and maintenance of the integrity of the blood-brain barrier. Astrocytes cover the outer surface of the basement membrane of brain capillaries with their perivascular feet, which are terminal expansions of cytoplasmic processes. In this way, they help to ensure that the passage of substances from the bloodstream into brain tissue is well regulated.
2. Form the glia limitans also known as the glial limiting membrane or glial limiting lamina, which is a largely impermeable barrier between the surface of the CNS and the pia mater (the innermost meningeal membrane) formed by the vascular feet of astrocytes.
3. Provide metabolic support to neurons by modulating the chemical composition of the interstitial fluid within the brain by regulating the exchange of various ions and molecules between the blood and the interstitial fluid.
4. Provide structural support and plasticity to the neuronal tissue of the CNS through its cytoskeletal network.
5. Replace damaged nerve cells through astrocytosis, which involves the proliferation of astrocytes to fill the space left by dead neurons.

6. Neuronal development of the fetal brain through the release of chemicals that establish and guide connections between neurons.
7. Control the diameter of the vessels with which they are in direct contact, releasing vasoactive substances that result in the dilation or contraction of the vessel.
8. Uptake and release of various neurotransmitters, such as glutamate and gamma-aminobutyric acid (GABA).
9. Release of inflammatory mediators.
10. Astrocytes also regulate the concentration of neurotransmitters and other substances that can potentially interfere with neuronal function, such as potassium.
11. Highly specialized astrocytes serve as neural stem cells (NSCs) that divide and give rise to new neurons, in a process called neurogenesis. During embryonic development, NSCs generate almost all neurons of the brain.
12. Astrocytes play an important role as a modulator of synaptic communication, with likely implications for higher brain functions (Pinto-Duarte *et al.*, 2019; UNESP, 2020; Cabral-Costa, 2023; FAPESP, 2023; Ken Hub, 2023; Abbott, 2024; Maestrovirtuale, 2024; UNIFAL, 2024).

Cerebral endothelial cells (CECs) and astrocytes are the main cells that make up the blood-brain barrier (BBB) and provide selectivity to the entry of substances into the brain through the action of the metabolic barrier. An imbalance in this selectivity predisposes the CNS to neurodegenerative diseases and cancer (Figure 3) (Abbott *et al.*, 2006; Abbott, 2024; CUSABIO Technology LLC, 2024; Maestrovirtuale, 2024).

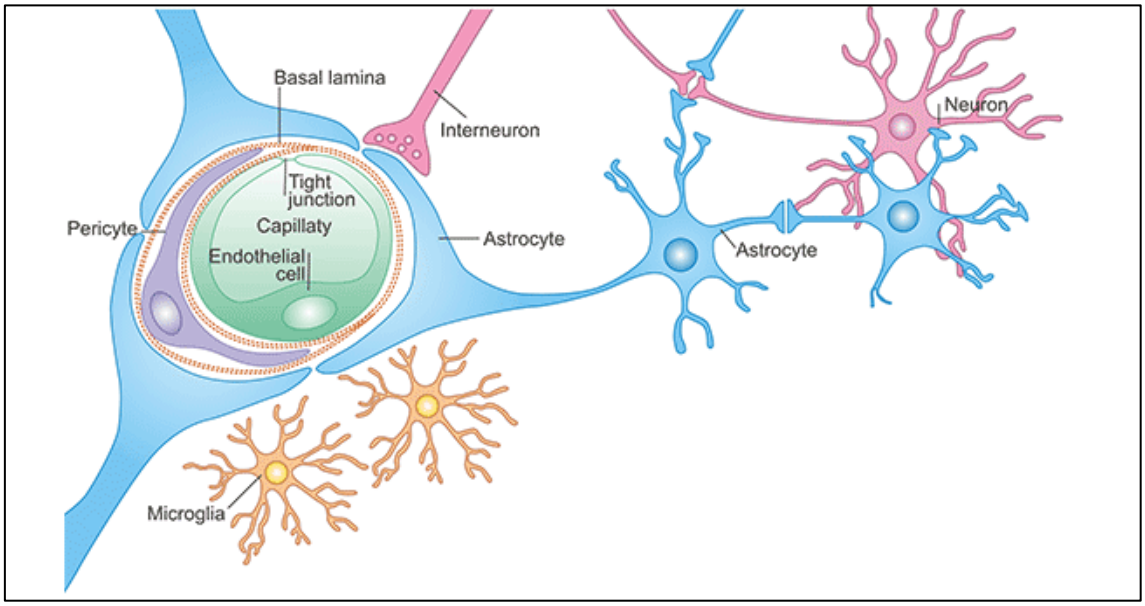

Figure 3: Cellular constituents of the blood-brain barrier

Sources: Doi: 10.1038/nrn1824 and https://www.cusabio.com/Neuroscience/Blood-brain-Barrier-Permeability.html

1.4. Types of astrocytes

Three types of astrocytes are differentiated by the cell lineage from which they come, that is, by the type of neuroepithelial cells from which they originate. Thus, we can distinguish between fibrous, protoplasmic, and radial astrocytes.

1.4.1. Fibrous: These astrocytes are located in the white matter of the nervous system, that is, in areas predominantly formed by myelinated axons. They are characterized by their low number of organelles (cellular subunits with differentiated functions).

1.4.2. Protoplasmic: Astrocytes contain many organelles and are the most numerous types of astrocytes. They are located mainly in the gray matter of the brain, composed mainly of cell bodies.

1.4.3. Radial: Glia plays a determining role during the process of cell migration since neurons "travel" through the nervous system based on this type of astrocyte. However, there are also radial glial cells that are active in adulthood, such as the Bergmann cells located in the cerebellum (Figure 4) (Jukkola *et al.*, 2013; UNESP 2020; Miranda-Negrón and García-Arrarás, 2022; Cabral-Costa, 2023; FAPESP, 2023; Ken Hub, 2023; Abbott, 2024; Maestrovirtuale, 2024).

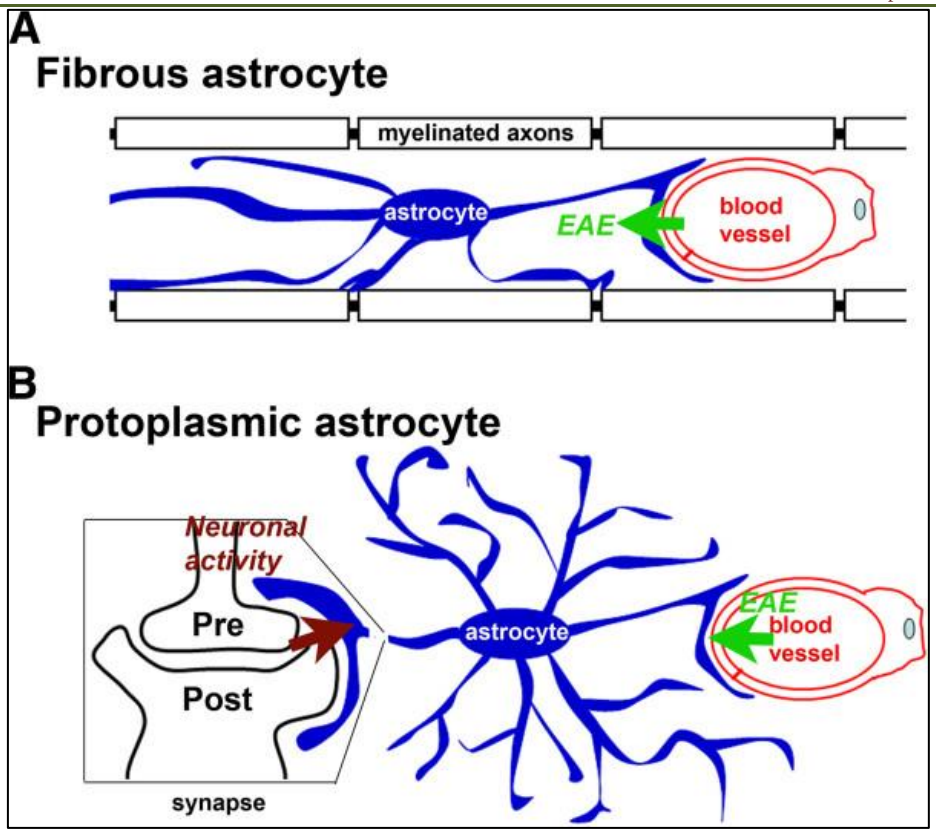

Figure 4: Diagram of regulation of fibrous and protoplasmic astrocytes by inflammation and neuronal activities. (A), Fibrous astrocytes in the WM with end feet contacting blood capillaries and nodes of Ranvier. (B), Protoplasmic astrocytes in the GM with end feet contacting blood capillaries and synapses
Source: https://www.researchgate.net/figure/Diagram-of-regulation-of-fibrous-and-protoplasmic-astrocytes-by-inflammation-and-neuronal_fig8_258765870

1.5. OBJECTIVE

This article aims to relate the characteristics and functions of astrocytes in the brain nutrition function, in the memory and learning process of stroke.

2.0. METHOD

Concerned with outlining a public profile of quality research in the area, we sought to answer these questions based on a literature review in the main journals in the area (national and international) classified by the Coordination for the Improvement of Higher Education Personnel (CAPES). To complement this analysis with other types of documents such as books, scientific journals, documents, and digital platforms, the following analysis steps were followed: (1) exhaustive reading of each article aiming at a global understanding and discovery of the approach used by its authors; (2) identification of the central ideas of each article; (3) classification of the ideas around core meanings; (4) comparison between the different core meanings present in the articles studied; (5) classification of the core meanings into broader axes (themes) around which the authors' discussions revolved; and (6) writing of interpretative summaries of each theme. After analyzing the content of the articles, we sought to establish a dialogue between the themes found and the literature that served as a basis for introducing the present study.

3.0. STUDIES CONDUCTED

3.1. How Astrocytes may be Related to the Process of Memory and Learning

Salk scientists find that astrocytes, long thought to be secondary players in the brain, are necessary for establishing long-lasting memories in mice. The classic view was that astrocytes' function was primarily to provide support for the most active neurons, helping to transport nutrients, clear away molecular debris, and hold neurons in place. Only more recently have researchers discovered that they may play other, more active roles in the brain through the release of gliotransmitters, but these remain largely mysterious (Sherwood *et al.*, 2017; Pinto-Duarte *et al.*, 2019; Salk News, 2019; Guan *et al.*, 2022).

It turned out that disabling the release of gliotransmitters in astrocytes reduced a type of electrical rhythm known as gamma oscillation, which is important for cognitive abilities. In this study, when researchers tested the learning and memory abilities of mice with deficient astrocytes, they found deficits restricted to their ability to discriminate novelty [Professor Terrence Sejnowski, head of Salk's Laboratory of Computational Neurobiology]. The new study looked for the first time

at the long-term memory of mice with disrupted astrocytes. They used genetically engineered animals lacking a receptor callexcfd type 2 inositol 1,4,5-trisphosphate (IP_3R2), which astrocytes rely on to release calcium for communication [Sejnowski] (Figure 5) (Sherwood *et al.*, 2017; Pinto-Duarte *et al.*, 2019; Salk News, 2019; Guan *et al.*, 2022).

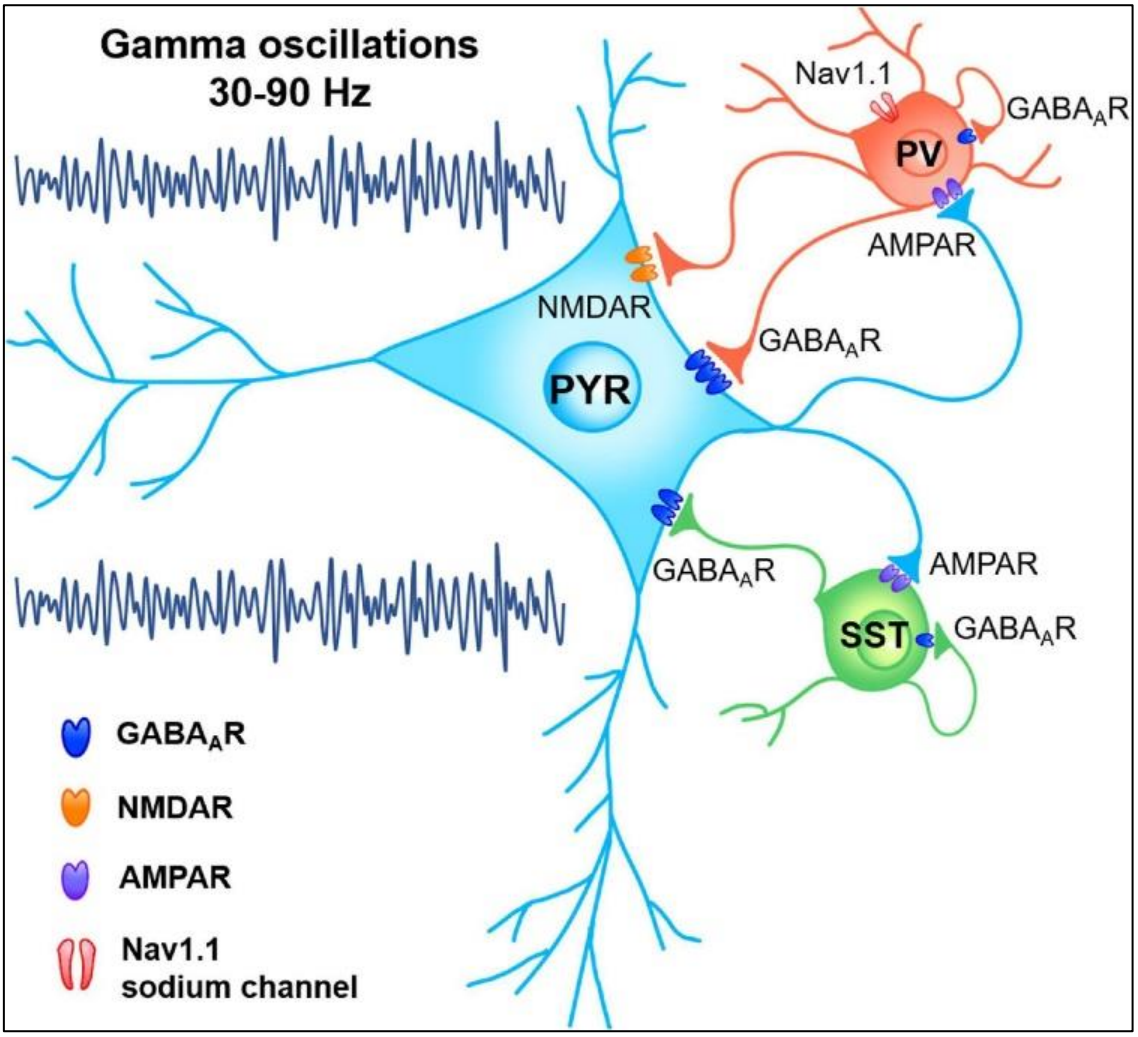

Figure 5: Network mechanism of gamma oscillations. Functional connectivity between pyramidal neurons (PYR) and inhibitory interneurons, including parvalbumin-expressing (PV) and somatostatin-expressing (SST) neurons, dynamically organized the synchronous oscillations in the gamma band through pyramidal-interneuron network gamma (PING) or interneuron network gamma (ING) mechanisms
Source: Doi: 10.3389/fncel.2022.962957

"The mice were given three different types of learning and memory challenges, including interacting with a novel object and finding the way out of a maze. In each case, mice lacking IP_3R2 showed the same ability to learn as normal mice. Furthermore, when tested 24 to 48 hours after each initial learning process, the mice with disrupted astrocytes could still retain the information by finding their way around the maze, for example. The results were consistent with what had been seen in previous studies. But when they tested the trained mice again 2 to 4 weeks later, they saw major differences the mice without the receptor performed much worse, making more than twice as many errors completing the maze" [Sejnowski] (Fiacco *et al.*, 2008; Lima, 2009; Goergen, 2014; Sherwood *et al.*, 2017; Pinto-Duarte *et al.*, 2019; FAPESP, 2023).

Synaptic morphological changes are associated with several neurodevelopmental disorders, including schizophrenia, autism spectrum disorders, and neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease. Astrocytes participate in some pathophysiological processes of these diseases through synapse regulation and other effects. Astrocytes influence the development of dendritic protrusions and synaptic plasticity during neural circuit development, while the link between this influence and human neurodevelopmental disorders is deepening (Figure 6) (Li, 2016; Gzielo and Nikiforuk, 2021; Liu *et al.*, 2021).

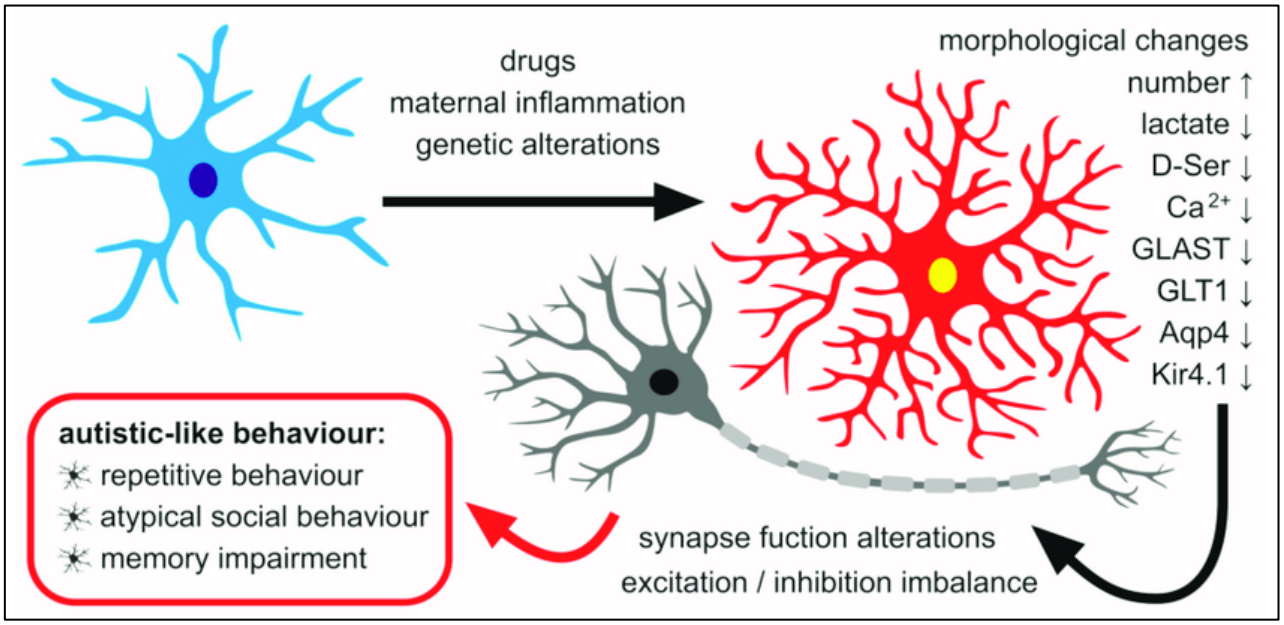

Figure 6: The possible role of astrocytes in the development of autism. Genetic mutations, prenatal exposure to some drugs, and prenatal inflammation affect astrocytic morphology and function. This may result in altered synapse function, imbalanced homeostasis between excitation and inhibition, and dysregulation of the nervous system. This, in turn, may lead to autism-like behavioral changes. D-Ser: D-serine; GLAST, GLT-1: glutamate transporters; Aqp4: aquaporin 4; Kir4.1: inwardly rectifying K+ channels
Source: Doi.org/10.3390/ijms222111544

3.2. Protein with Anti-Aging Action Combats Inflammation and Prevents Neuron Death

In a study, researchers suggest that klotho protein may act not only in the metabolism of neurons and astrocytes but is also an important component in the modulation of glial neuroinflammation. Thus, the therapeutic potential of klotho may be beneficial for pathological processes with neuroinflammatory factors. Aklotho is an anti-aging protein whose concentration increases significantly after birth and in adulthood, decreasing with advancing age, when there is a chronic inflammation known as "inflammaging". This unregulated, systemic, low-grade inflammation in the brain is associated with cognitive deficits and the progression of neurodegenerative diseases (Corrêa *et al.*, 2022; Muniz, 2023; Chen *et al.*, 2024).

"I was previously in a study on chronic kidney disease associated with neuroinflammation and we found that this klotho protein was reduced and this correlated with the onset of cognitive deficits" [Cristoforo Scavone, professor of the Department of Pharmacology of the Institute of Biomedical Sciences of the University of São Paulo (USP)]. Despite the good results, the authors warn that it is not clear whether klotho is the only mediator involved in the observed neuroprotective effect. However, the accumulated evidence justifies that its potential should be further elucidated (Figure 7) (Corrêa *et al.*, 2022; Prud'homme *et al.*, 2022; Muniz, 2023; Chen *et al.*, 2024).

3.3. Astrocyte Function Brain Nutrition

The primary function of mitochondria is to generate energy in the form of the molecule adenosine triphosphate (ATP). It also performs another crucial activity: the capture and storage of calcium in the form of Ca2+, a calcium ion that is essential for the functioning of the body. The researchers demonstrated that a protein called NCLX (an acronym for sodium-calcium exchanger), responsible for transporting calcium out of the mitochondria, modulates glycolytic flux (the breakdown of glucose to generate ATP) and the secretion of lactate (a product of the transformation of glucose into energy when there is not enough oxygen, a process called anaerobic glycolysis), shaping calcium signaling inside the astrocyte [Redoxoma: FAPES Research, Innovation and Dissemination Center (CEPID) João Victor Cabral-Costa and Alicia Kowaltowski] (Figure 8) (Fiacco *et al.*, 2008; Lima, 2009; Goergen, 2014; Cabral-Costa *et al.*, 2023; FAPESP, 2023).

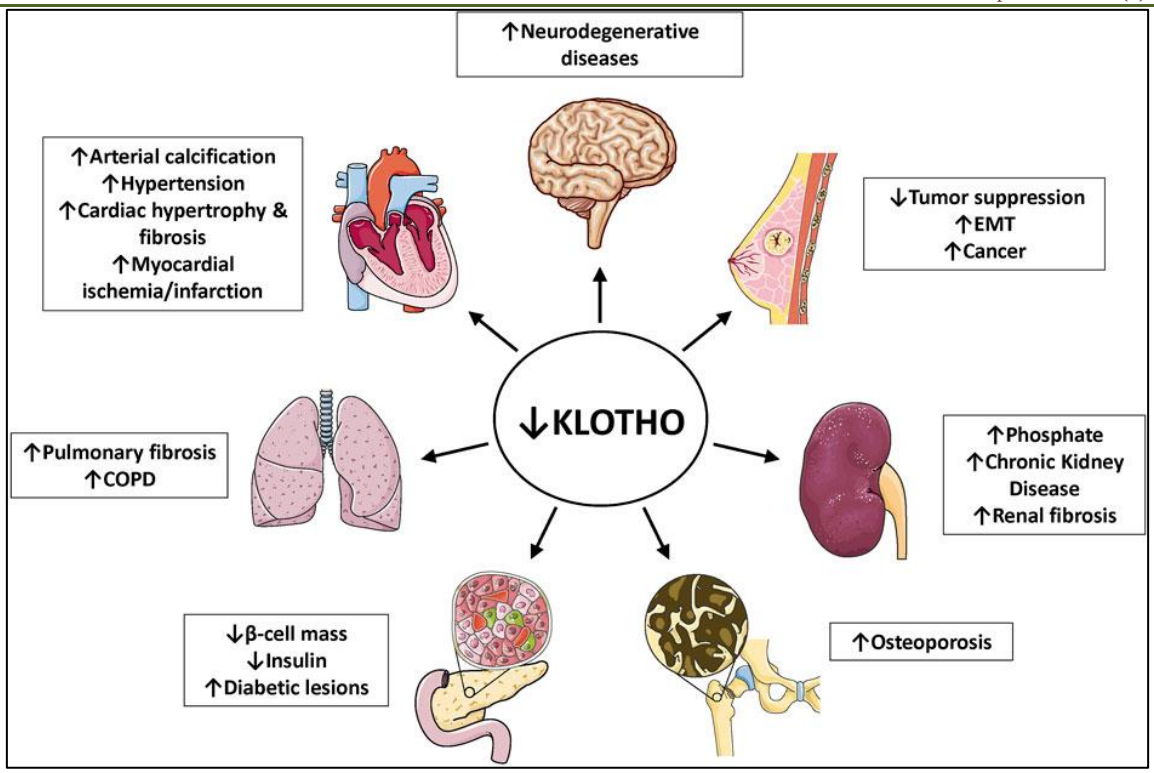

Figure 7: Klotho deficiency associated with multiple age-related diseases. As outlined in the captions, depressed Klotho levels are linked to hyperphosphatemia, chronic kidney diseases, multiple cardiovascular conditions, neurodegenerative diseases, several types of cancer, pulmonary fibrosis, COPD, bone disease and diabetes (reduced β-cell mass in the pancreas)

Source: Doi: 10.3389/fragi.2022.931331

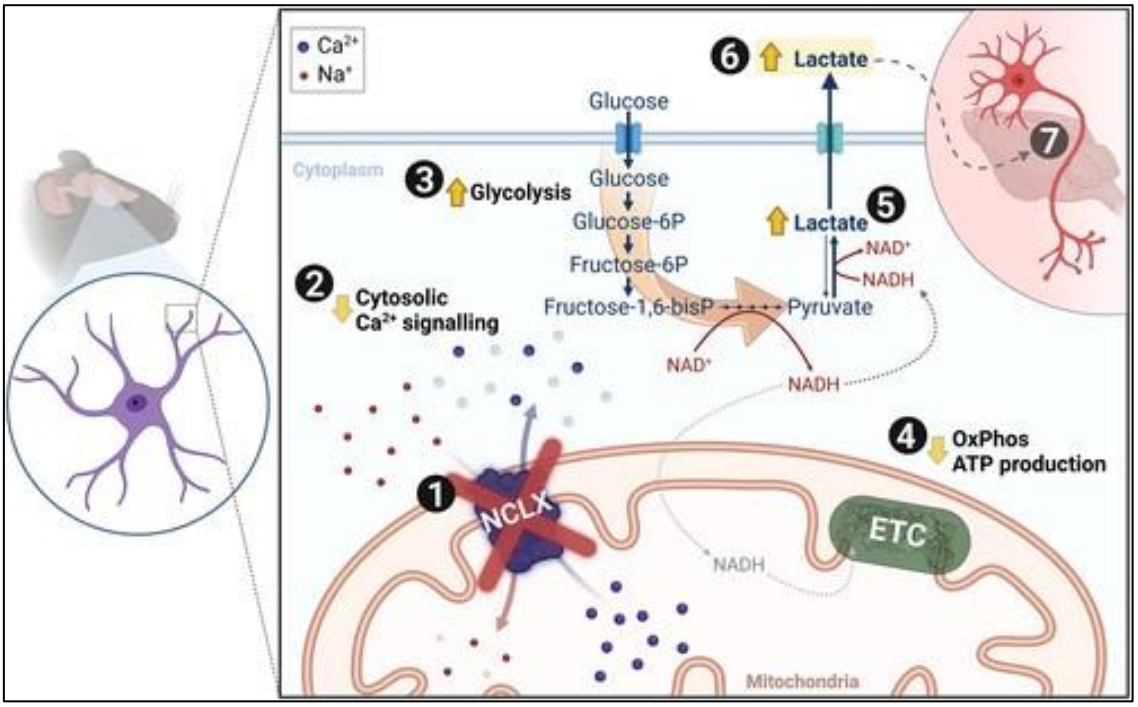

Figure 8: Schematic overview. In astrocytes, (1) inhibition/deletion of mitochondrial Na+/Ca2+ exchanger (NCLX) activity leads to (2) augmented cytosolic Ca2+ clearance. This results in (3) increased glycolytic flux; and (4) slightly decreased mitochondrial oxidative phosphorylation, leading to (5) increased lactate dehydrogenase (LDH)-mediated reduction of pyruvate to lactate. The resulting increased lactate in astrocytes (6) is secreted (7) and may contribute to enhanced behavioral performance in vivo. (ETC: Electron transport chain)

Source: https://doi.org/10.1111/jnc.15745

Thus, the work showed that NCLX can act in the control of brain metabolism, affecting the transport of lactate from astrocytes to neurons and, therefore, brain function [Redoxoma: FAPES Research, Innovation and Dissemination Center (CEPID) João Victor Cabral-Costa and Alicia Kowaltowski] (Fiacco *et al.*, 2008; Lima, 2009; Goergen, 2014; Cabral-Costa *et al.*, 2023). Astrocytes were once thought to be simple "helpers" to neurons, but over time they have been discovered to play a more active role in the brain. Astrocytes express ion channels, receptors, transmitters, and transporters, and therefore have mechanisms to detect and respond to neuronal activity. Astrocytes regulate synaptic plasticity by controlling the levels of neurotransmitters such as D-serine. D-serine acts as a co-agonist of NMDA receptors, modulating the strength and direction of synaptic connections, processes that are fundamental to learning and memory (Figure 9) (Raque *et al.*, 1999; Banerjee *et al.*, 2008; Araque and Navarrete, 2010; Rodrigues, 2022).

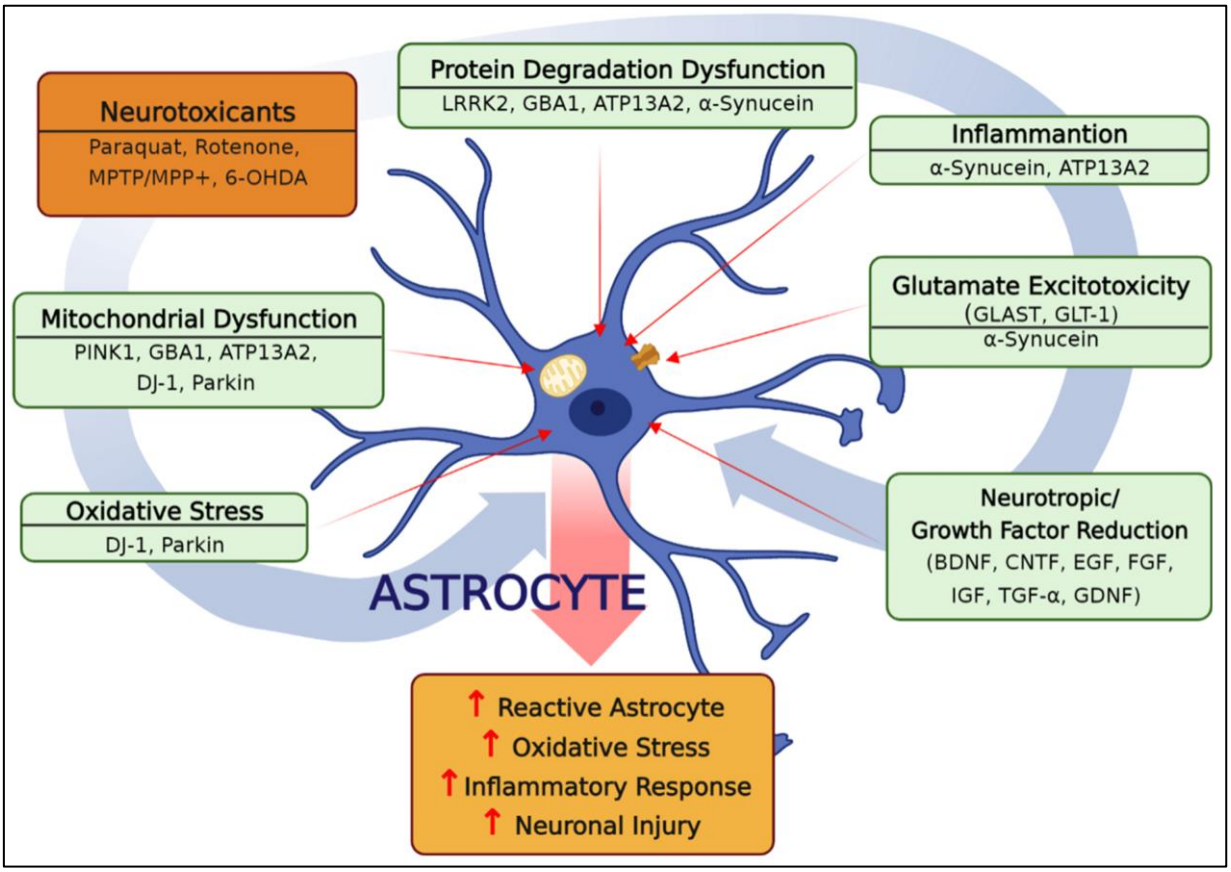

Figure 9: Astrocytes: The protectors and healers
Source: https://blog.mindbrainbodylab.com?utm_source=navbar&utm_medium=web

Astrocytes, she says, are support cells. "They isolate synapses, which are the spaces between neurons where information is transmitted from one cell to another, protect them in the event of a harmful stimulus, along with the cells of the brain's immune system, which are microglia, and also play a fundamental role in energy supply." The main source of energy for the brain is glucose, which reaches the organ through the bloodstream. "The blood-brain barrier controls the entry of nutrients into the nervous system, which has specific transporters for various nutrients, such as glucose, ketone bodies, a source of energy in fasting, and lactate," she points out [Researcher Ana Maria Marques Orellana, from ICB of USP] (Dorado, 2023).

"To avoid fluctuations dependent on the concentrations of substrates originating from the blood, there is a natural energy coupling between neurons and astrocytes," explains Ana Orellana. "The neuron captures the glucose and it will be used to generate energy immediately, without storage. The astrocyte, in turn, captures glucose, which is stored as glycogen, favoring a reserve"[Researcher Ana Maria Marques Orellana, from ICB of USP] (Dorado, 2023).

Brain energy metabolism requires the use of glucose via the glycolytic pathway and oxidative phosphorylation, which occur in a compartmentalized manner in different types of nerve cells. However, glucose is not the only energy substrate used by the brain; in some situations, such as hypoglycemic periods, the brain uses ketone bodies and lactate as alternative energy sources, demonstrating an ability to oxidize other energy substrates in addition to glucose (Raque *et al.*, 1999;

Stanley, 2001; Banerjee *et al.*, 2008; Vasconcelos, 2009; Aragona *et al.*, 2013; Smith, 2018).

Glucose transport to nerve cells requires the presence of specific transport proteins called GLUTs (glucose transporters), which transport glucose through facilitated diffusion. In brain tissue, three isoforms of the GLUT family participate in glucose transport: GLUT1-55kDa, present mainly in endothelial cells of the blood-brain barrier; GLUT1-45kDa, present in glial cells; and GLUT3, the predominant glucose transporter in neurons. Astrocytes can produce lactate in aerobic situations. Under these conditions, increased neuronal activity promotes the release of glutamate, which is co-transported to astrocytes with three Na+ ions through the glutamate transporter (EAAT1), activating the Na+/K+/ATPase pump and causing increased glucose uptake due to the increased cellular energy requirement (Figure 10) (Stanley, 2001; Banerjee *et al.*, 2008; Vasconcelos, 2009; Araque and Navarrete, 2010; Aragona *et al.*, 2013; Smith, 2018).

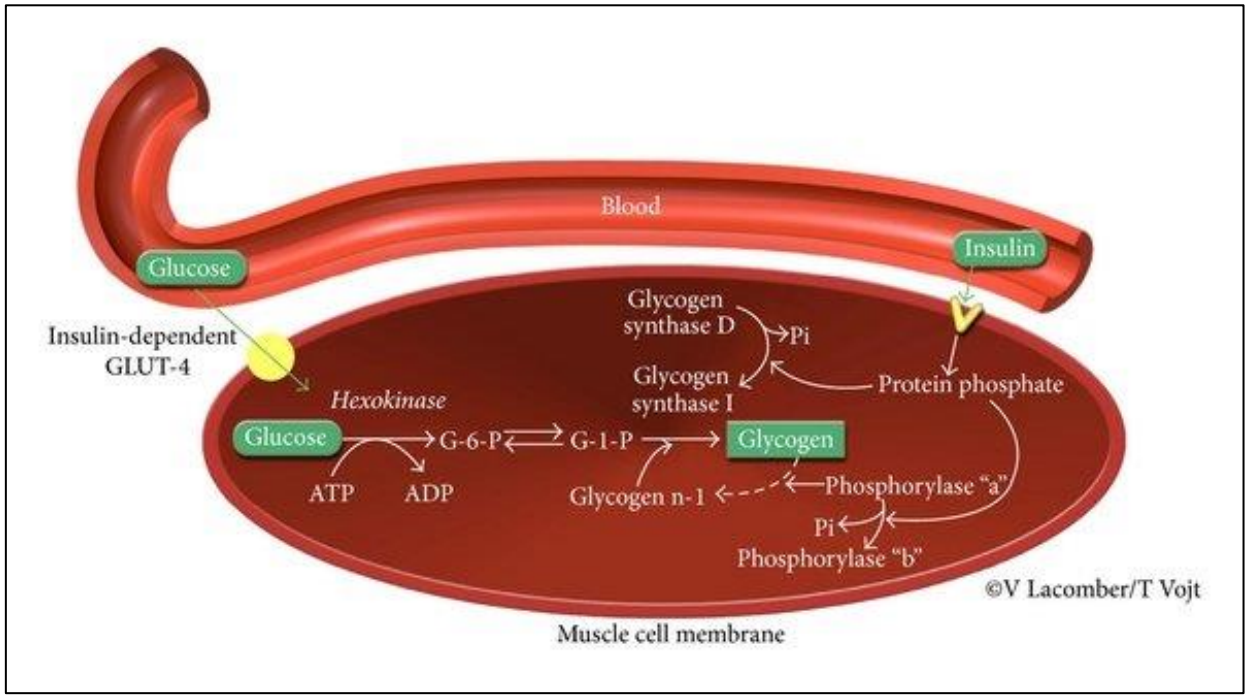

Figure 10: Biochemical pathways underlying glucose uptake and glycogen synthesis in the skeletal muscle after a high soluble carbohydrate diet. Insulin (1) activates GLUT4 translocation to enhance glucose uptake; (2) activates protein phosphatase, which converts glycogen synthase from its inactive form (D) to its active form (I); and (3) inhibits glycogenolytic enzymes such as phosphorylase a. G-6-P: glucose-6-phosphate; G-1-P: glucose-1-phosphate
Source: file:///C:/Users/USUARIO/Downloads/Expression_and_Regulation_of_Facilitative_Glucose_-1.pdf

Thus, astrocytes will preferentially transform glucose into lactate, which will be transported to neurons through monocarboxylate transporters. B vitamins, such as thiamine and niacin, help metabolize nutrients for the brain and obtain energy. Others, such as vitamins B12 and folate, can help protect against dementia by degrading homocysteine, a harmful substance that can lead to Alzheimer's disease. The brain's main source of energy is glucose, which is obtained from carbohydrate-rich foods (Raque *et al.*, 1999; Stanley, 2001; Banerjee *et al.*, 2008; Vasconcelos, 2009; Aragona *et al.*, 2013; Smith, 2018).

Neuronal activity is associated with reduced brain pH, astrocytes are responsible for rebalancing the pH to maintain equilibrium. Since lactate level is the main determinant of brain pH, neuronal activities are impacted by pH changes due to proton binding to various types of proteins, altering their structure and function in neuronal and non-neuronal cells of the brain. Lactate and pH can affect several types of epigenetic modifications, including histone acetylation, which is linked to histone acetylation and DNA methylation. Importance of pH homeostasis in normal brain function, the role of lactate as a key epigenetic regulatory molecule, and its contributions to brain pH abnormalities in neuropsychiatric diseases (Nohesara, 2024).

3.4. Top 5 Brain Nutrients; Learn about the Essential Nutrients to Help Keep your Brain in Shape

A. Lutein

This is a yellow-pigmented carotenoid found in all parts of the brain, and it helps with learning and memory. In addition, research has shown that the amount of lutein present in the eye is positively related to the speed of processing in the brain.

B. Omega-3 DHA

This omega-3 fat makes up 25% of the brain's fat, helping to reduce inflammation and improve

communication between brain cells. The main sources of DHA are fish with a higher amount of fat, such as salmon, tuna, and sardines.

C. B vitamins

This family of vitamins protects the brain in several ways. B vitamins, such as thiamine and niacin, help metabolize nutrients for the brain and obtain energy. Others, such as vitamins B12 and folate, may help protect against dementia by breaking down homocysteine, a harmful substance that can lead to Alzheimer's disease.

D. Vitamin D

Vitamin D does more than keep your bones and heart strong. It can also help keep you feeling better, as it helps your brain cells produce mood-regulating neurotransmitters like dopamine and serotonin.

5. Protein

Healthy muscles don't just keep you strong. They've also been linked to better cognitive abilities in older people.5 Protein provides the building blocks that preserve muscle mass, which is especially important since most people start losing muscle after their 40s. For optimal muscle health, aim for 25 to 30 grams of protein at each meal (Chang *et al.,* 2009; Steves *et al.,* 2016; Zamroziewicz and Barbey, 2016; Anjum *et al.,* 2018).

3.5. Stroke and Astrocytes

When the injury is severe, the expression of GFAP is significantly upregulated, and the cell body of astrocytes has a large number of periodicity and diffusion leading to overlap between cells. Astrocytes in protective cells will form glial scars between damaged areas and resistant tissues, which may play different roles in the progression of the disease. Transforming growth factor β (TGF-β) and bone morphogenic protein (BMP) are two members of this signaling pathway (Justicia *et al.,* 2000; Kajihara *et al.,* 2001; Senn *et al.,* 2014; Ceyzériat *et al.,* 2016).

By stimulating their receptors, the Smad family transcription factors in astrocytes can be activated. It has been proven that active BMP can activate Smad and promote astrocyte differentiation, and this effect can be eliminated by inhibiting BMP. TGF-β can also regulate astrocyte differentiation (Figures 11-13) (Justicia *et al.,* 2000; Kajihara *et al.,* 2001; Senn *et al.,* 2014; Ceyzériat *et al.,* 2016; Wang *et al.,* 2020; Dagonnier *et al.,* 2021; Shen *et al.,* 2021).

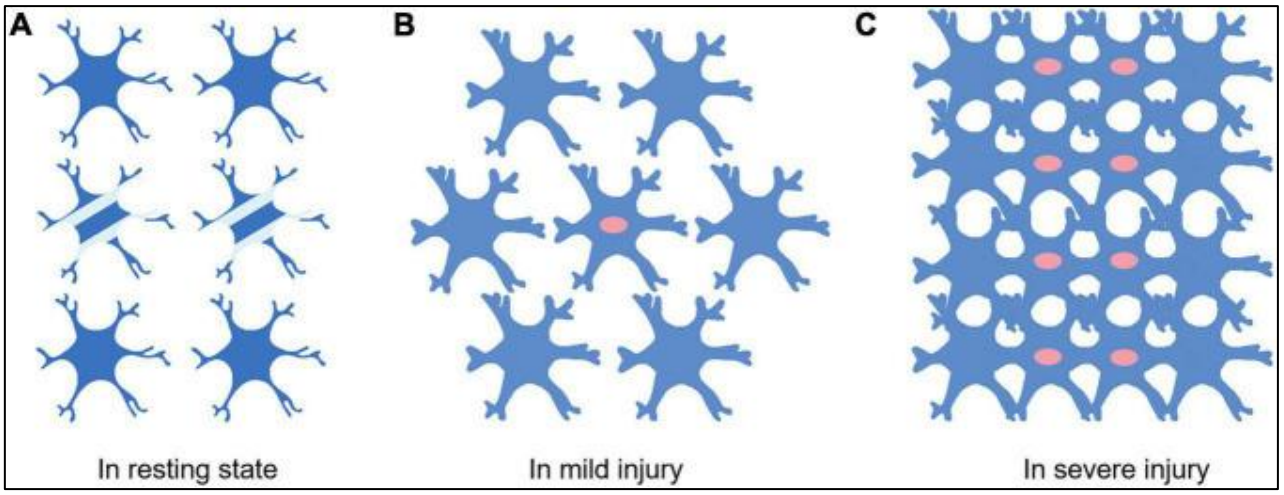

Figure 11: Differences of astrocytes in different extent of injury. (A) Astrocytes in the resting state. Not all astrocytes express detectable levels of GFAP (Two cells in the middle of A). There are clear and definite boundaries between cells. Little or no proliferation. (B) Most astrocytes express detectable levels of GFAP when the injury occurs. The astrocyte soma swells and proliferation begins to appear (The cells with red nuclei represent proliferating astrocytes). (C) Swollen astrocytes start proliferating massively. The boundaries between cells are destroyed

Source: Doi: 10.3389/fncel.2021.755955

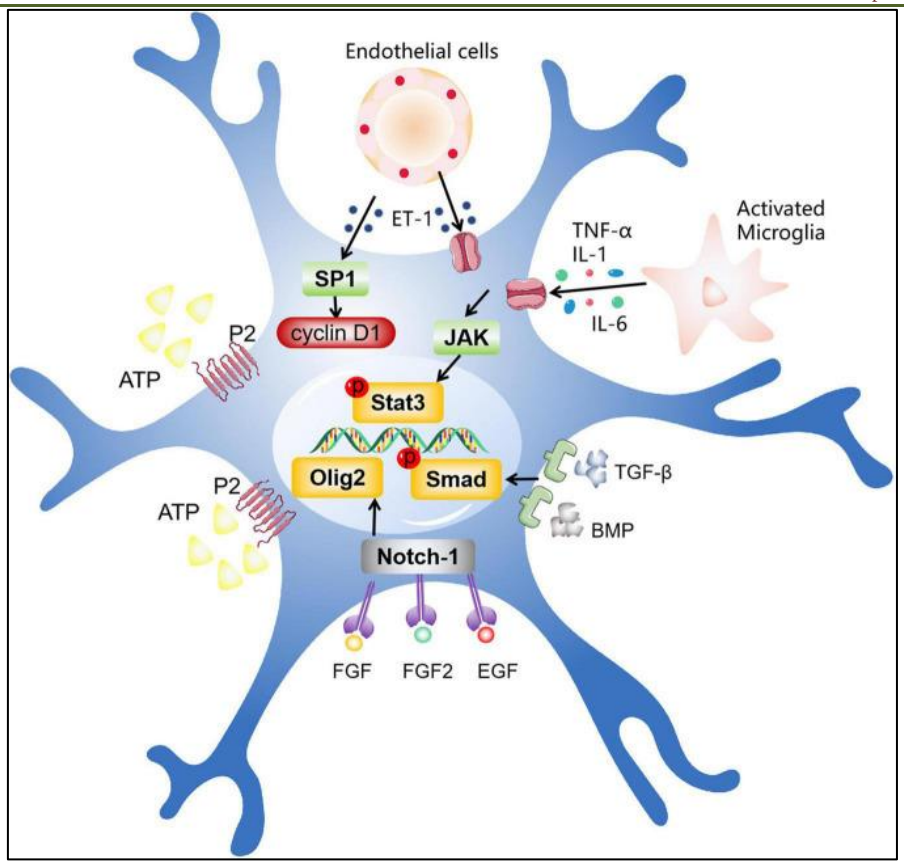

Figure 12: The intracellular mechanisms related to astrocyte activation. After ischemic stroke, different types of cells promote astrocyte activation by secreting various factors, including activated microglia, dead neurons, endothelial cells, and other cells. These factors act by entering the cell via multiple pathways, such as the JAK/STAT3 pathway, the Olig2 pathway, TGF-β/The Smad pathway, and other pathways
Source: Doi: 10.3389/fncel.2021.755955

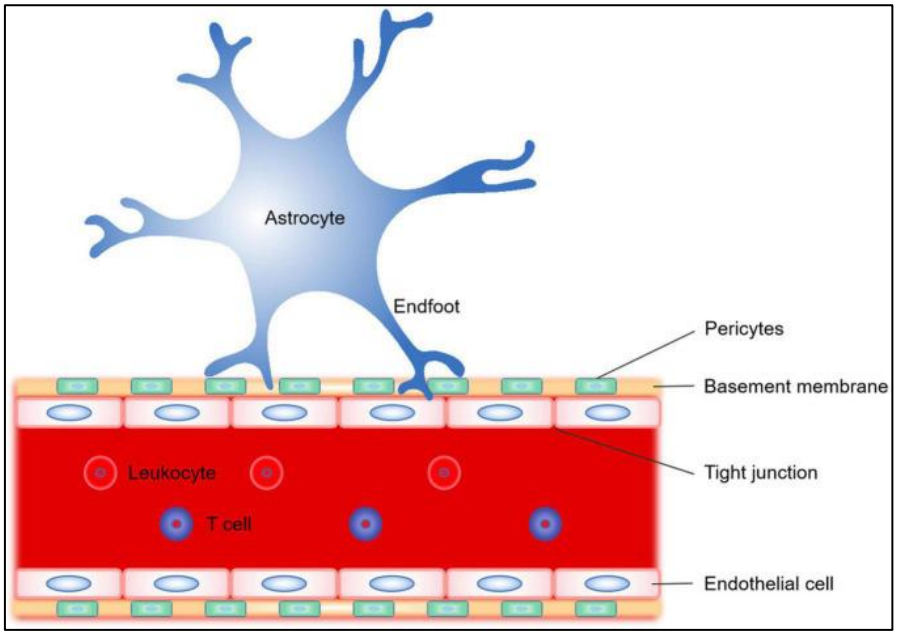

Figure 13: Schematic representation of the significant constituent structures of the blood-brain barrier (BBB). The BBB is a complex composed of astrocyte end foot, vascular endothelial cells, tight junction, basement membrane, and pericytes. The astrocytes regulate the homeostasis and function of BBB mainly by transporting different derived factors through their end foot
Source: Doi: 10.3389/fncel.2021.755955

4. CONCLUSION

They connect neurons to capillaries and the pia mater for nutrition. They also provide support and form a network for communication, healing, and maintenance of chemical balance. The transfer of molecules and ions is called vascular feet. Long and fewer extensions are in the white matter, called fibrous astrocytes; short extensions and more branches, and coarse aspects are in the gray matter, called protoplasmic astrocytes.

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