Neurología. 2015;30(2):119—129

NEUROLOGÍA

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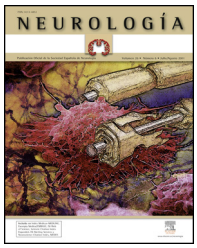

REVIEW ARTICLE

Astrocytes in neurodegenerative diseases (I): function and molecular description☆

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Received 10 December 2012; accepted 15 December 2012
Available online 19 January 2015

KEYWORDS
Astrocyte;
Neurodegeneration;
Glial fibrillary acidic protein;
Astrocytosis;
Glia;
Neurodegenerative diseases

Abstract
Introduction: Astrocytes have been considered mere supporting cells in the CNS. However, we now know that astrocytes are actively involved in many of the functions of the CNS and may play an important role in neurodegenerative diseases.
Development: This article reviews the roles astrocytes play in CNS development and plasticity; control of synaptic transmission; regulation of blood flow, energy, and metabolism; formation of the blood-brain barrier; regulation of the circadian rhythms, lipid metabolism and secretion of lipoproteins; and in neurogenesis. Astrocyte markers and the functions of astrogliosis are also described.
Conclusion: Astrocytes play an active role in the CNS. A good knowledge of astrocytes is essential to understanding the mechanisms of neurodegenerative diseases.

PALABRAS CLAVE
Astrocito;
Neurodegeneración;
Proteína ácida fibrilar glial;
Astrocitosis;

Astrocitos en las enfermedades neurodegenerativas (I): función y caracterización molecular

Resumen
Introducción: Los astrocitos han sido considerados como células de sostén en el SNC. Sin embargo, hoy día se sabe que participan de forma activa en muchas de las funciones del SNC y que pueden tener un papel destacado en las enfermedades neurodegenerativas.

☆ Please cite this article as: Guillamón-Vivancos T, Gómez-Pinedo U, Matías-Guiu J. Astrocitos en las enfermedades neurodegenerativas (I): función y caracterización molecular. Neurología. 2015;30:119—29.

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2173-5808/$ - see front matter

Glía;
Enfermedades neurodegenerativas

Desarrollo: Se revisan las funciones del astrocito en el desarrollo y plasticidad del SNC, en el control sináptico, regulación del flujo sanguíneo, energía y metabolismo, en la barrera hematoencefálica, regulación de los ritmos circadianos, metabolismo lipídico y secreción de lipoproteínas y en la neurogénesis. Asimismo, se revisan sus marcadores y el papel de la astrogliosis.
Conclusión: Los astrocitos tienen un papel activo en el SNC. Su conocimiento parece esencial para comprender los mecanismos de las enfermedades neurodegenerativas.

Introduction

Glial cells make up the largest part of the cells in the nervous system. Also known as glia (from the Greek word for glue), these cells have been evolutionarily conserved. The proportion of these cells in each different nervous system seems to correlate with the size of the animal: for example, we find 25% in fruit flies, 65% in mice, 90% in humans, and 97% in elephants.[1] Based on their shape, function, and location, glial cells are classified as follows: (1) microglia, the only glial cells of immune origin, which reach the brain through the blood during early development; (2) astrocytes; and (3) Schwann cells and oligodendrocytes, which form myelin layers around axons in the peripheral and central nervous systems, respectively. Some authors describe an additional special type of glial cells, glia-NG2, which receive synaptic input directly from neurons.[2] Astrocytes, accounting for 25% of the total brain volume, are the most abundant glial cells.[3] Whereas the respective functions of the microglia and oligodendrocytes are well-known (local defence and myelination), the astrocytes play a more enigmatic role. When they were first described by Ramón y Cajal, and in later works by Río-Hortega, they were considered mere supporting cells, but their function has been reconsidered in recent years. As scientists' understanding of these structures grew, they were found to be necessary elements in the maintenance of the microenvironment permitting proper function. A wide variety of specific functions has been attributed to these cells in the last 20 years. Molecular studies of these cells show that they play a key role in transmitting information in the nervous system. This 2-part review aims to analyse the function of astrocytes in mechanisms potentially at work in the most common neurodegenerative diseases.

Astrocyte morphology and organisation

Based on their shape, antigen phenotype, and location, astrocytes are classified into 2 major groups: protoplasmic and fibrous. Protoplasmic astrocytes are found in the grey matter and their processes contact both synapses —about 100 000 per astrocyte[4]— and blood vessels (Fig. 1). They have a rounded shape with several main branches that terminate in very ramified, uniformly distributed processes. Fibrous astrocytes are located in the white matter and they contact the nodes of Ranvier and the blood vessels. They are less ramified than protoplasmic astrocytes, and their processes are longer and more fibre-like. Although astrocytes occupy discrete domains and their processes do not overlap in adult brains, electron microscope analysis reveals that both subtypes establish gap junctions with the processes of neighbouring astrocytes. While this classification system is widely used, astrocytes form a very heterogeneous population containing many different subtypes. Furthermore, astrocytes even differ within the same region of the brain. This is not surprising when we consider that they must carry out their functions in specific regions of the nervous system.[1] For example, we find such specialised astrocytes as the retinal Müller cells and the Bergmann glia in the cerebellum.[5] The astrocytic cells in the subventricular zone (SVZ) belong to a subtype of astrocyte that is able to proliferate in the adult brain. Beginning in the postnatal period, astrocytes are arranged in the nervous system in an orderly manner with scarcely any overlaps, in parallel with vascular and neuronal territories.[6] In grey matter, only the distal ends of protoplasmic astrocytes intertwine to provide the

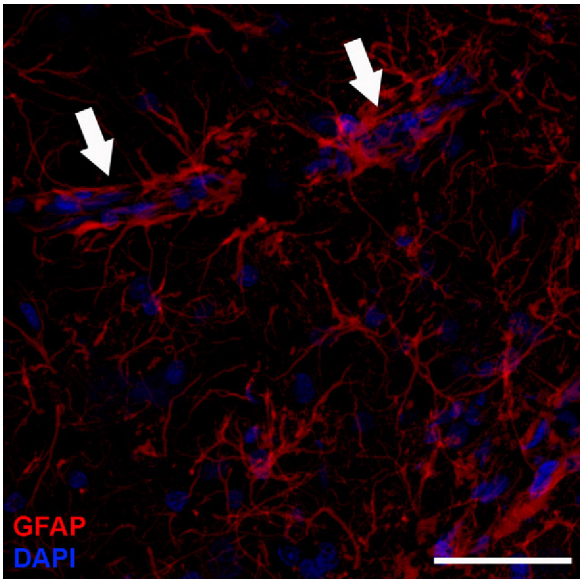

Figure 1 Astrocytes are distinguished by their starlike shape; cerebral capillaries are nearly completely surrounded by astrocytic endfeet (arrows). Immunohistochemical stain for GFAP (red: astrocytes; blue: nuclei). Confocal microscopy image. Bar = 70 μm.