IJAE
Vol. 119, n. 1 (Supplement): 142, 2014
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Astrocyte clasmatodendrosis affects clearance mechanisms of Aß-fibrils in the hippocampus of aged rats

Daniele Nosi[1], Daniele Lana[2], Maria Grazia Giovannini[2] , Sandra Zecchi Orlandini

[1] Department of Experimental and Clinical Sciences, University of Florence, 50134 Florence, Italy
[2] Department of Health Science, University of Florence, 50139 Florence, Italy

Aging is frequently accompanied by a low-grade pro-inflammatory condition which is considered a prodrome of Alzheimer Disease (AD). Indeed a common event of aging and AD is the deposition of beta amyloid (Aß) fibrils in the central nervous system, that has been associated to cognitive decline also in normal aging. Identifying traits of amyloid aggregates are the irreversibility of their molecular interactions, the ability to propagate from one cell to another and resist to clearance mechanisms [1]. We previously reported that, in aged rats, astrocyte clasmatodendrosis promote neuron to neuron propagation of Aß-fibrils and, therefore, their prion like spread. Clasmatodendrosis is a phenomenon described in astrocytes that consists in the loss of their distal processes. It's known that astrocytes constitutively remove Aß-fibrils from neurolemma with their cytoplasmic processes and, in pathological conditions, this activity may cause their necrosis. Moreover, they regulate microglial activity in the central nervous system. Although microglial cells are involved in Aß-fibril clearance, they have also been associated to neuronal cell death in Alzheimer Disease. In this work we found that clasmatodendrosis is associated with a decrease of astrocyte activity of Aß fibril clearance in the pyramidal layer and affects microglial phagocytic activation in the hippocampus of aged rats. To discriminate immunofluorescence signals from autofluorescence typical of amyloid aggregates on confocal acquisitions, we designed a specific method of linear unmixing. Moreover, multiphoton microscopy analyses were implemented with an innovative method of fluorescence lifetime analysis (FLIM/Phasor), suitable to discriminate multiple fluorescences. On the whole our data suggest that clasmatodendrosis consistently affects clearance mechanisms of Aß fibril in the central nervous system and foreshadow new strategies in the development of therapeutical protocols against AD.

Reference

[1] Brundin P et al. (2010) Prion-like transmission of protein aggregates in neurodegenerative diseases. Nat Rev Mol Cell Biol 11: 301–307.

Keywords

Astrocytes, clasmatodendrosis, Aß-fibril spread, immunofluorescence, microglial cells.