MITOCHONDRIAL ULTRASTRUCTURAL DEFECTS IN REACTIVE ASTROCYTES OF ALZHEIMER'S MICE HIPPOCAMPUS

Laura Trujillo-Estrada1, Elba Lopez-Oliva1, Juan Jose Fernandez-Valenzuela1, Elisabeth Sanchez-Mejías1, Marina Mejias-Ortega1, Marisa Vizuete2, Javier Vitorica2 and Antonia Gutierrez1

1. Facultad de Ciencias, Universidad de Málaga, Dpto. Biología Celular, Genética y Fisiología. Instituto de Investigación Biomédica de Málaga (IBIMA). Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED).

2. Facultad de Farmacia, Universidad de Sevilla, Dpto. Bioquímica y Biología Molecular. Instituto de Biomedicina de Sevilla (IBIS). Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED).

Alzheimer's disease (AD) is a complex neurodegenerative condition that causes progressive memory loss and dementia. In AD brains astrocyte become reactive potentially contributing to cognitive decline. Astrocyte reactivity is a highly complex phenomenon with remarkable morphologic and molecular phenotype changes, and the role of astrocytes in the development of AD is still unknown. Astrocytes are the prevalent glial cells in the brain and have a large number of functions aimed at maintaining brain homeostasis including regulation of brain energy metabolism, maintenance of the blood-brain barrier, ion homeostasis, synaptic activity and plasticity, among many other functions. Any disruption regarding the normal roles of astrocytes can result in morphological and functional changes that ensue in pathological consequences. Mitochondrial dysfunction is an early event in the pathogenesis of AD, although most studies have focused on neurons and little is known about the functional characteristics and the dynamics of astrocyte mitochondria. We had performed an ultrastructural analysis using transmission electron microscopy in the hippocampus of amyloidogenic (APP/PS1) and tauopathy (P301S) mice. Our results show structural alterations in mitochondria that include double membrane rupture, cristae loss, and fragmentation together with a loss of their circularity. Since mitochondrial morphology is directly related to mitochondrial fusion/fission processes, the ultrastructural changes observed in astrocyte mitochondria in these amyloidogenic and tauopathy models suggest dynamic abnormalities in these organelles that may lead to deficits in astroglial function compromising their capability to maintain brain homeostasis and support neuronal energy metabolism and survival. A better understanding of cell type-specific mitochondrial dysfunction as a pathological feature of AD might hold great potential for the exploration of novel molecular targets for therapeutic development.

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