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Editorial

Mitochondria: Strategic Point in the Field of Alzheimer's Disease

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Alzheimer's disease is the most common cause of age-dependent cognitive decline composing a tragic epilogue in senility. A substantial number of cellular and biochemical mechanisms contribute in shaping the multifactorial pathogenetic background of the disease. In the neuropathological profile of Alzheimer's disease, selective neuronal loss [1], synaptic alterations [2], tau pathology [3], extracellular deposits of polymers of Aβ peptide [4], inflammatory responses [5] and morphological alterations of the cell organelles [6] are the most common phenomena in light and electron microscopy.

Morphological alterations of mitochondria even in the early stages of Alzheimer's disease underline the crucial role that mitochondrial structural changes and dysfunction play in the pathogenesis of Alzheimer's disease [7] and other neurodegenerative diseases, which are associated with oxidative alteration, calcium dysregulation, synaptic loss and apoptosis.

In Alzheimer's disease mitochondria may be the target for Amyloid Precursor Protein (APP) [8] and Aβ peptide [9], which may induce impairment of mitochondrial dynamics [10], increasing oxidative stress [11], decreasing energy production and affecting synaptic plasticity [12]. In addition, deficits in mitochondrial function may affect APP, presenilin 1 and presenilin 2, which are closely related with the pathogenesis of Alzheimer's disease [13], aggravating the course of the disease.

The mitochondrial dysfunction may be initiated many years prior to clinical phenomenology of Alzheimer's disease [14], resulting in gradual synaptic degeneration, given that synaptic mitochondria play a crucial role in maintaining synaptic function and plasticity [15]. It is important to underline that mitochondrial alterations are associated with synaptic loss in AD patients, even before amyloid aggregations are detected [16]. Morphological and morphometric studies revealed that at early stages of AD the number of mitochondria in synaptic components is considerably decreased and their morphology changed substantially [17,18].

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Recent studies revealed alterations in mitochondrial fission and fusion, due to increased Aβ peptide interaction with the mitochondrial protein Drp 1 [19], inducing increased mitochondrial fragmentation, impaired axonal transport of mitochondria, synaptic degeneration [20] and activation of apoptotic process, given that mitochondria fission and fusion are critical processes for mitochondrial health [21]. In addition, over expression of tau protein inhibits kinesin-dependent trafficking of mitochondria, clustering them in the perikaryon [22], decreasing the number of dendritic and synaptic mitochondria with serious consequences on synaptic plasticity [23,24], since mitochondrial transport has a high impact on synaptic homeostasis [25]. Normally mitochondrial motility and accumulation are harmoniously coordinated, since mitochondria are mainly transported to regions where the necessity for energy production and consume is particularly high, as it occurs in the synapses, which have high energy demand, for maintaining neuronal communication [26].

Therapeutic strategies targeting mitochondria may be beneficial in the initial stages of Alzheimer's disease. Thus protection to mitochondria by inhibition of mitochondrial β-oxidation [27], and therapeutic application of mitochondrial enhancers and molecules supporting the Electron Transport Chain (ETC) might play a positive role in a prodromal stage of Alzheimer's disease [28]. In experimental level modulation of mitochondrial complex I activity proved to be beneficial in multiple animal models of familial Alzheimer's disease [29]. Blockade of Cyclophilin D, which is a part of the mitochondrial permeability transition pore, may enlarge the therapeutic perspectives at the initial stage of Alzheimer's disease [30]. Controlling mitophagy may also ameliorate the clinical phenomena in some phenotypes of Alzheimer's disease [31].

In the spectrum of nanotechnology [32] mitochondria-targeting ceria nanoparticles as antioxidants may be beneficial in Alzheimer's disease [33].

In the ongoing research and the continuous endeavors to contribute therapeutically in Alzheimer's disease mitochondria remain a strategic point in the field.

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