MITOCHONDRIAL CALCIUM REGULATION IN ALZHEIMER`S DISEASE

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Background. Calcium ions (Ca^{2+}) play an essential role in neuronal function, contributing to synaptic transmission, interneuronal communication, and neuroglial interactions. Mitochondria regulate the intracellular homeostasis of Ca^{2+}, and disruption of this balance, as seen in Alzheimer's disease, promotes neuronal apoptosis and cerebral atrophy.
Objective of the study. To identify disturbances in Ca^{2+} homeostasis within nerve cells that contribute to the development of Alzheimer's disease, with the goal of improving diagnosis and developing effective treatment strategies.
Materials and Methods. To achieve the proposed objective, a literature review was conducted using 10 bibliographic sources, drawing data from electronic libraries such as PubMed, MedScape, Hindawi, and ScienceDirect.
Results. Under physiological conditions, Ca^{2+} enters the mitochondria through voltage-dependent ion channels (VDAC) at the level of the outer mitochondrial membrane and then traverses the inner membrane via the mitochondrial calcium uniporter. The efflux of Ca^{2+} from mitochondria is carried out by the $Na^{+}/Ca^{2+}/Li^{+}$ exchanger, thus maintaining ionic balance. The transfer of Ca^{2+} between the endoplasmic reticulum (ER) and mitochondria occurs via mitochondrial membrane junctions, formed through the interaction of IP_3 receptors (IP_3Rs) with VDAC, mediated by glucose-regulated protein 75, a molecular bridge that facilitates this interaction. In Alzheimer's disease, β-amyloid oligomers and presenilin mutations (PSEN1 and PSEN2) upregulate IP_3Rs, increasing Ca^{2+} release from the ER to the mitochondria. Additionally, the C99 cleavage product of amyloid precursor protein promotes the stabilization of ER–mitochondria coupling via the mitofusin-2 protein, enhancing Ca^{2+} influx into mitochondria. This mitochondrial Ca^{2+} overload induces the opening of the mitochondrial permeability transition pore (mPTP). Once open, mPTP allows the uncontrolled release of ions, reactive oxygen species, and pro-apoptotic and pro-necrotic factors from the mitochondrial matrix into the neuronal cytoplasm, thereby contributing to cell death and the neurodegenerative processes characteristic of Alzheimer's disease.
Conclusion: Maintaining calcium ion (Ca^{2+}) homeostasis is essential for normal neuronal function. In Alzheimer's disease, disruption of Ca^{2+} flux contributes to mitochondrial dysfunction and cell death. A detailed understanding of these processes is crucial for elucidating the pathogenesis of Alzheimer's disease and for developing new therapeutic strategies targeting mitochondrial