AMYLOID B-PRECURSOR PROTEIN MODULATES THE PHOSPHORYLATION OF TAU

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The molecular mechanisms that cause AD are still unknown. The leading theory in the AD field, the “amyloid hypothesis”, foresees soluble Aβ peptides as the toxic species responsible for neurodegeneration, while gliosis and hyperphosphorylated tau represent secondary damaging events caused by Aβ. In the last ten years it has been proposed a parallel theory, complementary to the “amyloid hypothesis”, in which is the APP that, acting as a cell surface receptor, modulates yet unclear cell signals, whose alteration may disrupt the neuronal homeostasis, cause neuronal impairment and re-activate cell-cycle in post-mitotic neurons resulting in neuronal death. In this regard, we show that the overexpression of APP induces the phosphorylation on Tau residues which are known mitotic and pathogenic phosphoepitopes on tau and NFTs. Moreover we observe that the overexpression of APP modulates the redistribution of the ratio between the nuclear and cytoskeletal pools of tau, a physiological process likely related to cytoskeletal stability, cell motility and cell cycle progression. Altogether our data provide a link between APP processing and intracellular signals linked to the mitotic phosphorylation of tau. We hypothesize that the occurrence of these events in postmitotic neurons would lead to cell death.