Brain aging and neurodegenerative diseases : a problem of signals

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Ca2+ is an ubiquitous intracellular messenger involved in the control of a variety of cellular functions as diverse as contraction, secretion, fertilization and death. To insure specificity to Ca2+ signalling, a multiplicity of mechanisms have been developed, based on amplitude, duration and subcellular localization of the Ca2+ changes. Compelling evidence has been obtained in the last decade demonstrating the key role of different organelles in shaping cytosolic Ca2+ signals and in controlling its consequences for cell pathophysiology. In this contribution I will concentrate on a few unanswered questions related to cellular and animal models of human diseases, in particular in models of Alzheimer disease due to mutations in Presenilins (PS), key components of the γ secretase complex, i.e. the enzyme responsible for the production of the amiloidogenic peptides from APP. I will discus some recent results suggesting that PS isoforms differently modulate intracellular Ca2+ homeostasis and in particular the ER- mitochondria Ca2+ dependent crosstalk.