The antioxidant N-acetylcysteine prevents the mitochondrial fragmentation induced by soluble amyloid-? peptide oligomers

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Background: Soluble amyloid-? peptide oligomers (A?Os), which are centrally involved in the pathogenesis of Alzheimer's disease, trigger Ca 2+ influx through N-methyl-D-aspartate receptors and stimulate reactive oxygen species generation in primary hippocampal neurons. We have previously reported that A?Os promote Ca 2+ release mediated by ryanodine receptors (RyR), which in turn triggers mitochondrial fragmentation. We have also reported that the antioxidant N-acetylcysteine (NAC) prevents A?Os-induced Ca 2+ signal generation. Objectives: To determine if RyR-mediated Ca 2+ release activated by the specific agonist 4-chloro-m-cresol (4-CMC) induces fragmentation of the mitochondrial network, and to ascertain if NAC prevents the mitochondrial fragmentation induced by A?Os and/or 4-CMC. Methods: Mature primary rat hippocampal neurons were incubated for 24 h with sublethal concentrations of A?Os (500 nM) or for 1-3 h with 4-CMC (0.5-1 mM), ±10 mM NAC. Mitochondrial morphology was assessed