ROLE OF OXIDATIVE STRESS IN THE NEURONAL DAMAGE INDUCED BY Aß FIBRILS

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Introduction: Amyloid ß-peptide (Aß) is triggering Alzheimer's disease by inducing neuronal cell death. Aß fibrils have been reported to produce H₂O₂ but different receptors and calcium channels have been also proposed as Aß cytotoxic effectors.

Aims: Our main goal is to demonstrate that oxidative stress is a major neurotoxic mechanism in the damage induced by Aß fibrils.

Methods: Yeasts, neuronal cell lines and neuronal primary cultures were challenged with Aß fibrils. We measured cell viability (MTT reduction), apoptosis (TUNEL method and caspase-3 activity) and expression of modified proteins (Western Blot and immunofluorescence).

Results: We found a reduction in the cell viability in yeasts when challenged with Aß40 fibrils. It was similar to that found with H₂O₂ treatment. Consistently, we have found that the presence of metal chelators prevented the Aß cytotoxicity in human neuroblastoma cells. We obtained that trolox prevent the apoptosis of mouse hippocampal neurons and avoided caspase 3 activation by Aß fibrils. Furthermore we demonstrated that trolox maintained the vesicular transport integrity in neurons challenged with Aß. Finally, we found that GSH prevented the formation of translational modifications (oxidation and glycation) of proteins induced by Aß in neuroblastoma cells.

Conclusion: Our data support that oxidative stress is a major cytotoxic mechanism induced by Aß, and confirm that antioxidants protect neurons from the Ab fibrils damage.

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