APPROACHES TO PROTECT AGAINST NITRO-OXIDATIVE DAMAGE TRIGGERED BY AMYLOID β-PEPTIDE


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Introduction: Alzheimer’s Disease (AD) is a neurodegenerative process characterized by amyloid β-peptide (Aβ) deposits in brain. There are evidences that nitro-oxidative stress is directly involved in Aβ neurotoxicity which induces peroxynitrite generation. It causes protein nitrotyrosination impairing its physiological function as it has been reported with triose phosphate isomerase (TPI).

Aims: The study on different strategies to protect against Aβ-induced neurotoxicity.

Methods: Neuronal primary cultures and neuroblastoma cell lines were assayed by MTT reduction (cell viability), MCB fluorescence (GSH levels), western blot and immunofluorescence (protein nitrotyrosination and denitrase activity).

Results: We show that brain derived neuronal factor (BDNF) and neurotrophin-3 (NT-3) protect neurons against Aβ and H₂O₂ but nerve growth factor (NGF) can not protect it. In fact, it is known that BDNF and NT-3 activate antioxidant intracellular defenses, mainly reduced glutathione (GSH) whereas we have found that NGF does not modulate GSH. In order to prevent peroxynitrite formation, we can not inhibit NO due to its essential physiological role, but we can protect against peroxynitrite toxicity with trolox, a water soluble analog of vitamin E. A more plausible strategy would be to reverse the nitrotyrosination. We report the existence of denitrase activity in human neuroblastoma cells that partially denitrates nitro-TPI.

Conclusion: Our data show different strategies such as neurotrophins and an unidentified denitrase enzyme that should be addressed as protective therapeutic approaches against Aβ in AD.

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