Beta-amyloid (1-42)-induced learning and memory deficits in mice: involvement of oxidative burdens in the hippocampus and cerebral cortex.

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We have demonstrated that oxidative stress is involved, at least in part, in beta-amyloid protein (Abeta)-induced neurotoxicity in vivo [Eur. J. Neurosci. 1999;11:83-90; Neuroscience 2003;119:399-419]. However, mechanistic links between oxidative stress and memory loss in response to Abeta remain elusive. In the present study, we examined whether oxidative stress contributes to the memory deficits induced by intracerebroventricular injection of Abeta (1-42) in mice. Abeta (1-42)-induced memory impairments were observed, as measured by the water maze and passive avoidance tests, although these impairments were not found in Abeta (40-1)-treated mice. Treatment with antioxidant alpha-tocopherol significantly prevented memory impairment induced by Abeta (1-42). Increased activities of the cytosolic Cu,Zn-superoxide dismutase (Cu,Zn-SOD) and mitochondrial Mn-superoxide dismutase (Mn-SOD) were observed in the hippocampus and cerebral cortex of Abeta (1-42)-treated animals, as compared with Abeta (40-1)-treated mice. The induction of Cu,Zn-SOD was more pronounced than that of Mn-SOD after Abeta (1-42) insult. However, the concomitant induction of glutathione peroxidase (GPX) in response to significant increases in SOD activity was not seen in animals treated with Abeta (1-42). Furthermore, glutathione reductase (GRX) activity was only increased at 2h after Abeta (1-42) injection. Production of malondialdehyde (lipid peroxidation) and protein carbonyl (protein oxidation) remained elevated at 10 days post-Abeta (1-42), but the antioxidant alpha-tocopherol significantly prevented these oxidative stresses. **Therefore, our results suggest that the oxidative stress contributes to the Abeta (1-42)-induced learning and memory deficits in mice.**

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