ATORVASTATIN PREVENTS HIPPOCAMPAL CELL DEGENERATION, NEUROINFLAMMATION AND OXIDATIVE STRESS FOLLOWING AMYLOID-1-40 ADMINISTRATION IN MICE

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The accumulation of amyloid-beta (Aβ) peptides in brain of human and rodents has been associated with activation of glial cells, neuroinflammatory and oxidative responses, and cognitive deficits. These oxidative changes leave glutamate transporters more vulnerable and result in excitotoxic damage. We evaluated the effects of atorvastatin, a HMG-CoA reductase inhibitor, in molecular and behavioral alterations induced by a single intracerebroventricular injection of aggregated Aβ1-40 (400 pmol) in mice. An increased glial fibrilar acidic protein (GFAP) expression and cyclooxygenase-2 (COX-2) levels were observed by immunohistochemical analysis. Biochemical evaluation revealed an increased lipid peroxidation and impairment in glutathione antioxidant system. Neuronal degeneration was found in the hippocampus of Aβ1-40-treated mice. Aβ1-40 also induced a marked decrease in glutamatergic transporters (GLAST and GLT-1) expression and in L-[³H] glutamate uptake in mice hippocampus, in addition to spatial learning and memory deficits evaluated in the Morris water maze task. Atorvastatin (10 mg/kg/day v.o.) was administered after Aβ1-40 injection and through 7 consecutive days. Atorvastatin treatment was neuroprotective against cell degeneration induced by Aβ1-40, reducing inflammatory and oxidative responses and increasing the expression of glutamatergic transporters. On the other hand, atorvastatin did not reverse the cognitive impairments and failed to alter the hippocampal glutamate uptake in Aβ1-40-treated mice. These results reinforce and extend the notion of the potential neuroprotective action of atorvastatin against the neuronal toxicity induced by Aβ1-40. In addition, our findings suggest that the spatial learning and memory deficits induced by Aβ peptides in rodents may not be entirely related to neuronal damage.