Introduction: Epidemiological evidence suggests that the use of certain antihypertensive drugs may decrease the incidence of Alzheimer’s disease (AD).

Aim: To evaluate the effects of the antihypertensive propranolol, a β-adrenergic antagonist, on the expression and activity of Insulin Degrading Enzyme (IDE). IDE is the principal protease involved in the degradation of both insulin and the beta-amyloid peptide (Aβ).

Methods: IDE was measured after propranolol treatment in both red blood cells and hippocampus from male Wistar rats, in SH-SYSY cells and in red blood cells obtained from healthy humans. IDE levels and activity were measured by western blotting and a fluorescent commercial assay kit respectively. To check the effects of enhanced IDE expression on Aβ toxicity, hippocampal primary neurons were incubated with Aβ (8 µM) and propranolol (1 µM and 10 µM) and cellular survival was measured by MTT assay. Insulin levels were measured by Elisa.

Results: IDE levels were significantly enhanced by administration of propranolol in all experimental systems used. In red blood cells, IDE activity was also increased by 40% after propranolol treatment (10 µM, 7 days of incubation). In primary cell culture, Aβ induced 35% of cell death, and this toxic effect was significantly prevented by propranolol. Insulin levels were not modified by the treatments.

Conclusions: Propranolol treatment, by increasing IDE activity, may decrease the levels of the beta-amyloid peptide without affecting insulin levels. Therefore, propranolol could exert a protector effect against progression of AD neuropathology, independent of blood pressure-lowering activity.