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Effects of Pravastatin on neurogenesis after cerebral ischemia in rats

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As a member of the hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins) with structural homology to HMG-CoA, Pravastatin competitively inhibits HMG-CoA reductase activity, and reduces cholesterol content in the liver which leads to negative-feedback low-density lipoprotein (LDL) receptor up-regulation and subsequent lowering of total serum cholesterol levels. Recent studies suggested that statin treatment reduces the incidence of stroke by 25% to 30%. In addition, statins may also improve stroke outcome in humans. Although statins apparently have a neuroprotective effect, few study focused on the neurogenesis and cell immigration induced by statins.

We used the filament method for temporary middle cerebral artery occlusion and administered Pravastatin or saline post-ischemically at subsequent time points: at 6 hours, and then at every subsequent day until 14 days after tMCAO. Animals were sacrificed at day 14. Neurological outcome was investigated by using a neuroscore, the beam balance test and the rotarod test. Cholesterol and triglycerides were investigated by blood samples analysis. Infarct area was calculated by MAP2 staining. Neurogenesis was evaluated by triple staining (BrdU, DCX, NeuN). The aim of this study was to test whether low dose (1mg/kg) of Pravastatin enhances neurological recovery after stroke onset, and whether it induces neurogenesis in the dentate gyrus, subventricular zone and striatum of the rat brain.

In conclusion, low dose of Pravastatin administration early after stoke onset and on subsequent days appears relatively safe and promotes neurological recovery in ischemic stroke. Pravastatin induces cell proliferation in the dentate gyrus and subventricular zone, and increases the number of migration cells in the striatum. These benefits are independent of its cholesterol-lowering property.