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Simvastatin Effects On Brain and Behavior in Animal Model

J. Vevera[1], Z. Fi?ar[1], T. Nekovárová[2], K. Vale?[2]

[1]Psychiatry, First Faculty of Medicine Charles University, Prague 2, Czech Republic ; [2]Institute of Physiology, Academy of Sciences of the Czech Republic, Prague, Czech Republic

Introduction: Simvastatin and other HMG-CoA (3-hydroxy-3-methylglutaryl coenzyme A) reductase inhibitors (statins) have been demonstrated to reduce mortality and the risk of major cardiovascular events. However, their neuropsychiatric adverse effects have not been sufficiently studied.

The aim of our study is to elucidate effect of long term application of simvastatin on cholesterol level in the brain, serotonin uptake, microviscosity of membranes, and behavior in animal model.

Methods: We have studied cholesterol content in amygdala; hippocampus and prefrontal cortex, serotonin (5-HT) uptake and mitochondrial respiration in platelets, membrane microviscosity in erythrocytes, and behavioral changes in elevated plus maze in 6 male Long Evans rats in the control group and 6 rats in the simvastatin-treated group (30 mg/kg per day) after 2 and 4 weeks of treatment.

Results: Our results show: 1) lower cholesterol content in all tested brain regions in simvastatin treated group 2) decrease of SERT aktivity after 2 weeks of treatment compared to 4 weeks treatment 3) disturbed mitochondrial respiration and 4) higher number of entrances and the time spent in the closed arms in simvastatin group.

Conclusion

These results confirmed cholesterol-lowering effect of simvastatin in brain and harmful effect on cellular energy metabolism and further supported the hypothesis that lowering of plasma cholesterol after simvastatin treatments affects membrane fluidity and transmembrane transport of serotonin. Effects on behavior require additional testing to better explain observed changes in experimental tasks.

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