Influence of statins on mitochondrial biogenesis.

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Statins are ones of the most frequently prescribed drugs in the world. They lower cholesterol level and reduce risk of cardiovascular disorders by blocking a key enzyme in the malonate pathway. This pathway is also responsible for the synthesis of coenzyme Q, which is crucial for the proper functioning of the respiratory chain and the production of ATP by mitochondria. Brain cells are most susceptible to mitochondrial disorders due to their high energy requirements. We examined the effects of atorvastatin and simvastatin on mitochondrial biogenesis in Rattus norvegicus astrocytes and in the brains of young (3-month-old) and old (20-month-old) animals treated with statins for seven weeks. We used qPCR to determine mitochondrial copy number and examined the enzyme activities of citrate synthase (CS) and lactate dehydrogenase (LDH). Our studies showed that both statins stimulated mitochondrial biogenesis in astrocytes but not in brains of young animals. Mitochondrial DNA copy numbers were elevated by ~20% in astrocytes treated with both statins. Interestingly, in the brains of old statin-treated animals we observed an effect opposite to that observed in astrocyte cells. In old atorvastatin-treated rats, mitochondrial DNA copy number in the brain was reduced by ~26% compared to saline-treated control animals. No changes in the activity of CS and LDH enzymes were observed in any of the experiments. To explain this phenomenon, we will turn to mitochondrial staining experiments in astrocytes. Interestingly, the reduction in the number of mitochondrial DNA copies in the brains of old animals may indicate that the effect of statins on mitochondrial biogenesis is age-dependent.

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