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Accumulation of damaged mitochondrial DNA in tissues of aged rats and the impact of dietary restriction on this process

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The mechanism of accumulation of age-related damage in mtDNA remains unclear. It is unknown whether an increase in the levels of damaged mtDNA correlates with age. In this study, we analyzed the accumulation of mtDNA damage in organs of young and old rats and try to correlate them with the profile of oxylipins. In addition, we tested the possibility of reversing these changes by dietary restriction (DR). We showed that the mtDNA in brain structures (excluding the cerebellum) showed the most pronounced accumulation of age-related damage, similarly shown for the kidney, while the liver, testes and lungs were less susceptible to age-related accumulation of mitochondrial damage. DR prevented age-related accumulation of mtDNA damage in the cerebral cortex and reduced it in the lungs and testes. We also observed changes in the number of mtDNA copies, and these alterations were also tissue-specific. There was a tendency to an age-related decrease in the number of mtDNA copies in the striatum and its increase in the kidneys. DR contributed to an increase in the amount of mtDNA in the cerebellum and hippocampus. Analysis of the profiles of polyunsaturated fatty acids (PUFA) and oxylipins in old and young rats showed that DR reduces the synthesis of arachidonic acid and its metabolites. Thus, we have shown that aging significantly affects the amount of oxidative damage to mtDNA and oxidized fatty acid derivatives. DR significantly affects these processes, returning the studied parameters to those in young rats.

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