

# Reduced food intake in old mice can no longer improve health

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Mice become healthier through a change in diet if they start early in life and are fed this way into old age. Credit: MPI f. Biology of Ageing/ Lisa F. Drews

Reduced food intake helps both animals and humans to improve health in old age and can prolong life. But when do you have to change your diet to achieve this benefit in old age? Scientists from the Max Planck Institute for Biology of Ageing, the Excellence Cluster for Ageing Research at the University of Cologne, the Babraham Institute in

Cambridge and UCL have now shown that mice only become healthier if they start food reduction early and eat less before entering old age. The scientists conclude that healthy behavior must be established earlier in life in order to improve health in old age and extend lifespan.

How can we stay fit and healthy in old age for as long as possible? Researchers into aging have a simple answer: eat less and healthily. But when do you have to start and is it enough if you only manage to do this for a short time? To investigate this, researchers led by Linda Partridge, Director at the Max Planck Institute for Biology of Ageing, in an [animal study](#) have put young and [old mice](#) on a diet—with varying degrees of success.

## **Reduced food intake in old age has no beneficial effect**

Mice live longer and are healthier in old age if they are given 40 percent less to eat after reaching adulthood than animals who are allowed to eat as much as they want. The dieting mice are fed with [food](#) enriched with vitamins and minerals to prevent malnutrition. But if food intake is first reduced in mice first start eating less food when they are already seniors, the researchers observe little or no effect on the life expectancy of the mice. On the other hand, when mice are allowed to eat as much as they like after a period of reduced food intake, they have no long-term protection, so reduced food intake has to be sustained for mice to reap the benefits. Reduced food intake must therefore be implemented early and be sustained until the end of their lives to have positive effects on health in old age.

"One should establish healthy behaviors early in life. It may not be as good for your health to change your diet later in life. Health in old age is a lifelong affair", explains Linda Partridge from the Max Planck

Institute for the Biology of Ageing and UCL.

## Memory effect in fat tissue

But why do older mice no longer react to the change in diet? Oliver Hahn, first author of the study and doctoral student in the Partridge department, investigated [gene activity](#) in different organs. While the gene activity in the liver quickly adapted when mice are transferred to a restricted diet, the scientists observed a 'memory effect' in the fat tissue of older animals. Although the mice lose weight, the activity of the genes in the fat tissue is similar to that of the mice that continue to eat as much as they want. In addition, the fat composition in old mice does not change as much as in young mice. This memory effect mainly affects mitochondria, the cells' power houses, which play an important role in the aging process. Usually, reduced [food intake](#) leads to increased formation of mitochondria in fatty tissue. But the study showed that this is no longer the case when older mice are switched to a lower calorie diet. This inability to change at the genetic and metabolic levels may contribute to the shortened lifespan of these animals.

Michael Wakelam, co-corresponding author and Director of the Babraham Institute commented, "The experimental power of integrating data about lipid metabolism and metabolic pathways with tissue-specific understanding of gene expression in [mice](#) of different ages and diets has allowed us to demonstrate clearly the importance of a nutritional memory in contributing to healthy ageing."

**More information:** Oliver Hahn et al. A nutritional memory effect counteracts the benefits of dietary restriction in old mice, *Nature Metabolism* (2019). [DOI: 10.1038/s42255-019-0121-0](https://doi.org/10.1038/s42255-019-0121-0)

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