Flies fed restricted diet in early adulthood found to live longer

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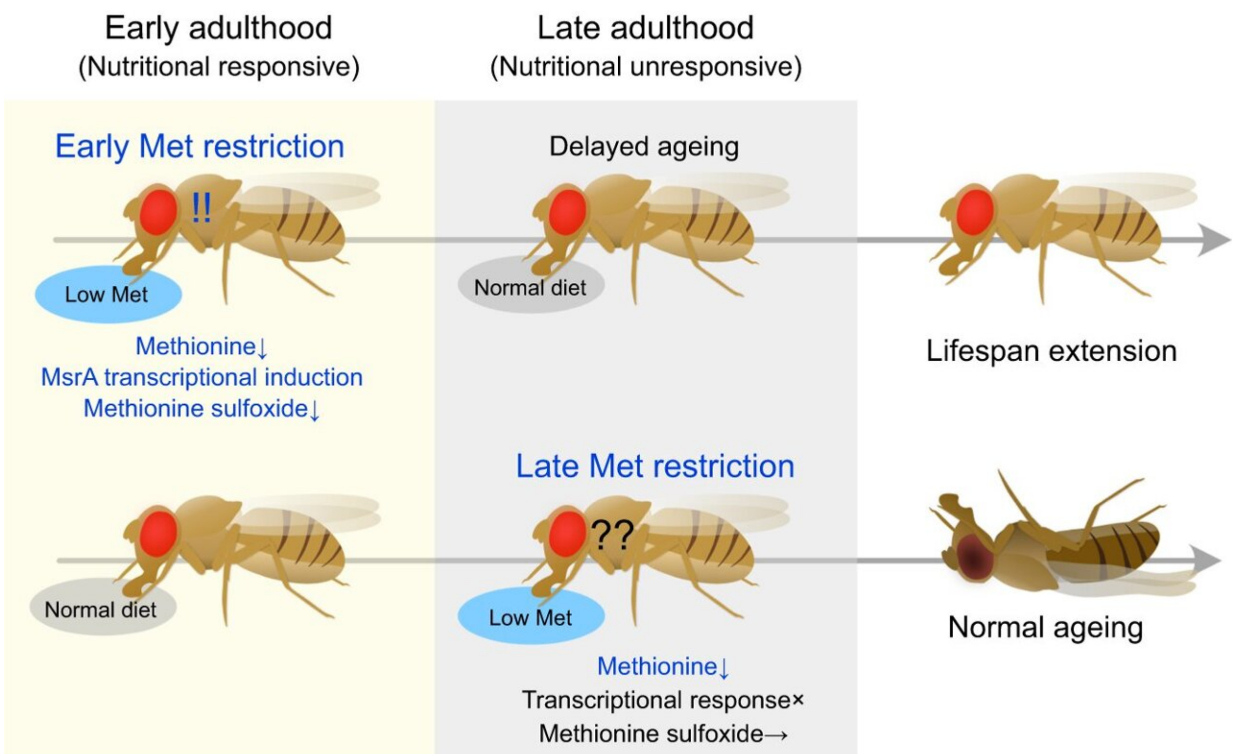

A model of lifespan extension by early Met restriction. Methionine restriction in young flies can induce MsrA and decrease MetSO level, leading to lifespan extension. This nutritional response wanes in older flies, despite internal methionine levels are decreased. Credit: *Nature Communications* (2023). DOI: 10.1038/s41467-023-43550-2

Fruit flies live considerably longer when fed a diet that limits consumption of a certain amino acid during early adulthood, RIKEN biologists have found. If a similar effect occurs in humans, it could allow people to live longer by eating restricted diets during certain stages of life. The study is published in *Nature Communications*.

Many studies have suggested that the life expectancy of animals can be extended by a lifelong diet of calorie restriction, but for many people this road to longevity is unpalatable.

However, similar benefits may be possible by a much more targeted dietary intervention, research by Fumiaki Obata of the RIKEN Center for Biosystems Dynamics Research and co-workers now suggests.

The advantages of caloric restriction are mainly associated with reduced protein consumption. In past experiments with female fruit flies, Obata and others have specifically linked these gains in lifespan to reduced intake of methionine, an amino acid that needs to be sourced from food since the body doesn't produce enough of it to maintain good health.

"But nobody actually knew at what life stage this amino acid affects the lifespan of animals," says Obata.

To address this question, Obata and co-workers compared the survival and health of female flies exclusively fed a methionine-reduced diet in early versus late adulthood.

Remarkably, flies fed the restricted diet for the first four weeks of adulthood experienced nearly the same longevity gains as flies that consumed reduced methionine throughout their entire lives—as much as 10% longer than flies on a standard diet. In contrast, the diet seemingly conferred little benefit when administered solely in late adulthood.

The researchers were also able to link diet-associated gains in longevity with boosted expression of an enzyme that biochemically "repairs" damaged byproducts of methionine, thereby boosting available reserves of this amino acid.

For reasons that remain unclear, male flies do not exhibit equivalent gains from methionine restriction, although it may have to do with the greater reproductive burden borne by females.

"Evolution is usually a friend of faster growth and greater reproductive activity at the cost of aging," says Obata. Higher protein and/or amino acid intake may favor the former processes, while restriction may shift the balance to slower aging.

It remains to be seen whether a similar pattern occurs in mammals, something that Obata and his team now intend to further examine.

Obata is intrigued by the possibility of an easier avenue to healthier aging for humans. "It's clearly much more preferable if we can shorten the length of dietary restriction and still reap the full benefit," says Obata. He is keen to further explore opportunities to achieve extended lifespan through targeted metabolic interventions delivered at earlier ages.

More information: Hina Kosakamoto et al, Early-adult methionine restriction reduces methionine sulfoxide and extends lifespan in Drosophila, *Nature Communications* (2023). DOI: 10.1038/s41467-023-43550-2