Metabolism

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Central metabolic activity is preserved in aged mice

Aging induces several changes in metabolism, including a decline in energy expenditure and increased adiposity. To date, most studies on aging have focused on changes in metabolite levels, while age-related changes in metabolic pathway activity (flux) remain understudied. A new study in mice combining the use of metabolomics and isotope tracing reveals that, although aging induces widespread changes in metabolite levels, major metabolic fluxes remain largely unchanged.

First, the investigators measured the serum concentrations of >170 metabolites in mature young (3–6 months) and aged (21+ months) mice using liquid chromatography-high-resolution-mass spectrometry (LC-MS), which confirmed widespread concentration changes with aging.

Next, to study the effects of aging on central metabolic activity, the researchers infused stable isotope-labeled metabolites into young and aged mice before collecting their blood and calculating circulating fluxes using LC-MS. They found that while the concentrations of 3-hydroxybutyrate, lactate, serine and many essential amino acids were significantly altered with aging, none of these metabolites showed altered flux at the whole-mouse level. Only the glutamine flux was subtly but significantly increased in aged mice.

Given that several metabolic features of aging are also associated with obesity, the investigators also measured metabolite levels and circulatory fluxes in young obese (ob/ob) mice (3–5 months). The findings show that major circulating fluxes were increased in ob/ob mice compared to age-matched wild-type mice, including the fluxes of glucose, lactate and several amino acids, which were not affected by aging.

Altogether, this study suggests that the circulatory fluxes of core metabolites are well preserved with age (but not with obesity), while pathways outside of core metabolism are more extensively disrupted. Future work is needed to further explore the age-related changes in certain fluxes like glutamine and their relevance to human aging.

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