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Fasting Induced Lipid Metabolic Changes in Drosophila Intestines during Aging

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Extended Abstract

Intermittent fasting (IF), characterized by alternating periods of fasting and feeding, has been shown to increase longevity in various organisms, such as fruit flies[1]. Previous work [2-3] indicated that older flies exposed to IF early in life display altered lipid content in the gut, which suggested a potential connection between lipid metabolism and longevity. However, direct visualization of lipid droplets and metabolic turnover in the gut remained limited. In this study, we applied deuterium oxide (D_2O) Stimulated Raman Scattering (DO-SRS) microscopy to investigate how a 3:1 fasting-to-feeding cycle affects gut morphology and lipid metabolism in aging Drosophila. By examining lipid droplet size, turnover rates, and unsaturated lipid ratios, we aimed to find the mechanisms underlying fasting-induced metabolic changes.

Female flies underwent a 3:1 fasting-feeding regimen until day 22 and then returned to normal feeding. From day 30 to 35, flies were given D_2O-enriched food, and midguts were dissected at day 35 for microscopy. DO-SRS imaging allowed detection of total and newly synthesized macromolecules by the CH and CD vibrational peaks. Protein and lipid turnover rates were calculated by comparing the CD signal to the total signal. Flavin and NADH fluorescence images were acquired to determine redox ratios. Ten representative cells per midgut were analyzed for lipid droplet size, unsaturated lipid ratio, and turnover rate. Data were averaged within each group and compared between fasting and control flies.

Fasted flies exhibited narrower midguts and larger lipid droplets than controls, which suggested reorganized gut structure and enhanced lipid storage. Lipid turnover was significantly higher in the lipid droplets in the fasting group, which showed rapid synthesis and breakdown of lipids. The unsaturated lipid ratio was also increased, indicating a shift toward potentially healthier lipid profiles. In contrast, protein turnover and redox ratios showed no significant differences. These findings support a connection between intermittent fasting and improved lipid metabolic flexibility in aging Drosophila.

Our data showed that intermittent fasting reshapes midgut structure and promotes intensified lipid metabolism in aging Drosophila. Increases in lipid droplet size, turnover, and unsaturation suggested that fasting modulated lipid metabolism in the gut, which may contribute to enhanced longevity in Drosophila. These results highlighted the role of targeted dietary interventions in modulating metabolic processes.

Keywords: Intermittent fasting (IF), deuterium oxide (D_2O) Stimulated Raman Scattering (DO-SRS) microscopy, fasting-induced metabolic changes.

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