A safflower oil-based high fat/high-sucrose diet modulates the gut microbiota and liver phospholipid profiles associated with early glucose intolerance in the absence of tissue inflammation

n-6 PUFA-rich diets are generally considered obesogenic in rodents. Here we examined how long-term intake of a high fat/high sucrose (HF/HS) diet based on safflower oil affected metabolism, inflammation and gut microbiota composition. We fed male C57BL/6J mice a HF/HS diet based on safflower oil - rich in n-6 PUFAs - or low-fat/low-sucrose (LF/LS) diet for 40 weeks. Compared to the LF/LS diet, intake of the safflower-based HF/HS diet only led to moderate weight gain, while glucose intolerance developed at week 5 prior to signs of inflammation, but concurrent with increased levels of linoleic acid and arachidonic acid in hepatic phospholipids. Intake of the HF/HS diet resulted in early changes in the gut microbiota, including an increased abundance of Blautia, while late changes coincided with altered inflammatory profiles and increased fasting plasma insulin. Analysis of immune cells in visceral fat and liver revealed no differences between diets before week 40, where the number of immune cells decreased in the liver of HF/HS-fed mice. We suggest that a diet-dependent increase in the n-6 to n-3 PUFA ratio in hepatic phospholipids together with gut microbiota changes contributed to early development of glucose intolerance without signs of inflammation. This article is protected by copyright. All rights reserved.

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