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The role of dietary fatty acids in the lipid metabolism of the liver and adipose tissue

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Abstract

Hepatic steatosis, or non-alcoholic fatty liver disease (NAFLD), is a pathophysiological condition characterized by fat deposition in the liver in patients without a history of alcohol abuse. NAFLD is currently identified as the hepatic manifestation of metabolic syndrome, which is associated with insulin resistance and central obesity. NAFLD is associated with undesirable and detrimental changes in lifestyle and is frequently a consequence of high fat, high caloric diet consumption and physical inactivity as well, as demonstrated in insulin-resistant individuals. Steatosis was also observed in a long-term study conducted in LDLR knock-out (KO) mice submitted to a high fat diet, and the liver fat accumulation was similar with polyunsaturated and saturated fatty acids. Independent of the type of fatty acids in the diet, a high fat diet strongly induces fat deposition in the liver. It is important to note that steatosis can be successfully reversed as demonstrated in obese mice with metabolic syndrome after switching to a normal fat diet.

The main fatty acid sources of liver triacylglycerols and plasma lipoproteins in NAFLD patients are non esterified fatty acids (NEFAs) derived from adipose tissue lipolysis. *De novo* lipogenesis (DNL) also contributes significantly to hepatic fat accumulation. In the fasting state, 26% of liver triacylglycerol in NAFLD patients were derived from *de novo* lipogenesis, which is several-fold greater than the 5% observed in healthy subjects. However, NAFLD patients failed to increase lipogenesis postprandially in response to a high fat diet, suggesting that their lipogenic capacity has reached the threshold. Westerbacka *et al*. investigated the main genes that were significantly up-regulated in the fatty liver of insulin-resistant subjects with NAFLD. They found an increase in genes involved in fatty acid trafficking, synthesis and storage as well as inflammation, such as PPAR-γ 2, the monocyte-attracting chemokines (i.e., MCP-1) and macrophage inflammatory protein-1 alpha (MIP-1□) and four genes associated with fatty acid metabolism acyl-CoA synthetase long-chain family member 4 (ACSL4), fatty acid binding protein (FABP4 and FABP5) and LPL. Curiously, among these genes, PPAR-γ2, FABP and LPL are normally expressed, especially in adipose tissue. The implications of the dietary fatty acids regarding the majority of these genes will be discussed. Regarding adipose tissue, dietary fat remarkably takes part both in the phospholipid composition of the adipocyte membranes and in the modulation of transcription of different genes involved in the processes of lipolysis and lipogenesis. Moreover, fatty acids greatly influence adipocyte regulation, as they affect the secretion of different adipokines and inflammatory biomarkers. High fat diet consumption is related to elevated triacylglycerol concentrations in adipose tissue, induction of metabolic stress, increases lipolysis and exacerbation of adipokine signaling. All of these situations culminate in an important inflammatory process. Additionally, western type diets are related to insulin resistance, greater adipose tissue fatty acids release and less glucose uptake elicited by an imbalance between cytokines and macrophage infiltration. An increase in plasma triacylglycerol concentration leads to ectopic fat deposition, especially in muscle, liver, and pancreas, thereby enhancing lipotoxicity and cellular apoptosis. The main mechanisms concerning the effects of dietary fatty acids on adipocyte metabolism are summarized.