Molecular Pathways of CLA-Induced Apoptosis under Different Fat based Diets in Obese Zucker Rats

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Conjugated linoleic acid (CLA) refers to the conjugated geometric and positional isomers of octadecadienoic acid, effective in reducing white adipose mass through molecular mechanisms not completely understood so far. Our experimental design included obese Zucker rats fed atherogenic diets with distinct fat origins, palm oil and ovine peritoneal fat, and supplemented with CLA (as a mixture of c9,t11 and t10,c12 isomers). We hypothesized that reducing weight properties of CLA are due to adipocyte apoptosis and saturated fatty acids from distinctive sources, vegetal and animal, alone or combined with CLA could modulate the apoptotic responses. No changes were found in adipose tissue depots weight, which is in line with the similar levels of apoptosis found in retroperitoneal fat. Yet, CLA reduced final body and liver weights. Interestingly, CLA had a contrasting effect on cell death in the liver, according to the dietary fat. Facing the palm oil diet, CLA increased hepatocyte apoptosis but reduced the apoptotic responses in rats fed animal fat. As saturated fatty acids are believed to induce apoptosis in the liver, most likely in an endoplasmic reticulum (ER) stress-dependent manner, we firstly tested this hypothesis by investigating the c-Jun N-terminal kinase (JNK) signalling pathway. Secondly, a possible involvement of the extrinsic pathway induced apoptosis was investigated, through Fas cell death receptor. The higher apoptotic levels found in CLA vegetal based diet seemed to be dependant on the extrinsic pathway without contribution of ER stress. On the contrary, the ovine fat group with CLA had higher disruption of ER homeostasis and subsequent activation of JNK pathway. Taken together, these findings reinforce the role of PUFAs, and in particular of CLA, as regulators of the ER stress pathway of apoptosis in the liver. In addition, they highlight the importance of fatty acid composition of matrix diets, as key factors in apoptotic signalling pathways activation.

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