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Effects of Mild Caloric Restriction on Lipid Metabolism and Inflammation in Liver and Adipose Tissue

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Obesity is associated with dysregulation of lipid metabolism and chronic inflammation, which contributes to the increased risk of many diseases including cardiovascular disease. Genetic, environmental, and dietary factors are responsible for the development of obesity. Reduced caloric intake combined with increased physical activity is the best way to achieve the weight reduction. Calorie restriction itself has been reported to have a beneficial effect of delaying the aging process and increasing life span in mammals. However, many calorie restriction models have employed the extreme reduction (more than 30%) of calorie intake. We investigated the impact of mild calorie reduction (about 15%) and obesity on expression of genes related to lipid metabolism and inflammation in liver and adipose tissue.

Seven week old C57BL/6N mice were fed high fat diet (60% energy fat, HFD group) ad libitum, control diet (10% energy fat, Control group) ad libitum, or reduced amount (15% less) of control diet (CR group) for 16 weeks. Triacylglycerol and cholesterol levels were measured from serum and liver tissue. Serum adipokines, hepatokine, and free fatty acids were determined. Expression of genes related to lipid metabolism (*Ppar γ* , *Srebf-1c*, *Fasn*, *Fabp1*, *Ppara*, *Cpt1a*, *Ahsg*) were determined from the liver tissue. Expression of genes involved in inflammation (*Mcp-1*, *Il-6*, *Il-1 β* , *Tnf- α* , *Socs3*) were measured from the liver and adipose tissue.

Serum and liver TG and cholesterol levels were significantly lower in the CR group compared with the Control and HFD

groups, while serum free fatty acid levels were significantly higher in the CR group compared with the other two groups. Liver expression of *Ppara* and *Cpt1a* did not differ among groups. Liver mRNA levels of *Ppar γ* and *Srebf-1c* were significantly higher in the HFD group compared with the CR and Control groups.

Liver and adipose tissue *Mcp-1* mRNA levels were significantly lower in the CR group compared with the Control group. Adipose tissue mRNA levels of *Mcp-1*, *Il-6*, *Tnf- α* and *Socs3* were significantly higher in the HFD group than in the Control and CR groups. Expression of *Lepr* in the liver was significantly higher in the CR group compared with the Control and HFD groups, but, this difference was not observed in the adipose tissue.

In conclusion, mild calorie restriction can reduce lipid accumulation and expression of inflammatory markers in the liver. Mild calorie restriction was effective in lowering expression of inflammatory cytokines in adipose tissue. Mild calorie restriction seemed to result in higher hepatic leptin sensitivity.

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