

## **„Changes in insulin sensitivity during a controlled weight cycle in healthy men: Impact of energy balance, glycemic index and carbohydrate intake“**

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Energy intake and consumption of refined carbohydrates (CHO) have increased over the past decades, while at the same time the incidence of metabolic disorders such as type 2 diabetes has risen. Studying the effect of modifications in energy balance, as well as diet composition on early alterations in glucose metabolism and insulin sensitivity in healthy subjects, may add to prevent nutrition-related diseases. Therefore, the present thesis examined the impact of i) controlled, consecutive periods of overfeeding, caloric restriction and refeeding ( $\pm 50-60\%$  of energy requirement), as well as ii) modifications in CHO-intake and glycemic index during the refeeding phase on changes in insulin sensitivity and associated parameters. The study population consisted of healthy men (aged  $25.4 \pm 3.5$  y, BMI  $23.4 \pm 2.0$  kg/m<sup>2</sup>) who were assigned to high vs. lower CHO-intake (50 vs. 65 energy %) comprising lower fibre, high GI vs. high fibre, low GI foods.

One to three weeks of energy deficit / excess induced significant alterations in insulin action: caloric restriction increased, and both overfeeding and refeeding decreased fasting and postprandial insulin sensitivity, with compensatory changes in insulin secretion. The refeeding-induced decrease in insulin sensitivity could be diminished by consumption of low GI, high fibre foods, especially at a lower CHO-intake (i.e. low glycemic load). Daylong glycemia during refeeding was higher with consumption of high GI foods, and was further raised by a high CHO-intake. When compared with lower CHO-intake, a high CHO-intake resulted in an increase in liver fat and fasting serum triglyceride levels with refeeding. At the end of the weight cycle, liver fat and fasting triglyceride levels remained elevated above baseline values and inversely correlated with insulin sensitivity.

During the weight regain period, a diet low in GI, rich in fibre, and moderate in CHO content (i.e. low glycemic load) may have favorable effects on daylong glycemia, insulin sensitivity and liver metabolism. In addition, a large demand on the insulin sensitivity-insulin secretion dynamics under the different feeding regimens was associated with increased weight gain. From a practical point of view, consumption of high-fibre, low glycemic load foods might therefore not only add to prevent a clustering of metabolic risk factors, but possibly also to body weight regulation in the long-term. A better insight into metabolic regulation will ultimately help to improve dietary recommendations to prevent nutrition-related metabolic disorders such as obesity, type 2 diabetes and cardiovascular disease.