The effect of intermittent fasting on insulin sensitivity – mechanism for exercise?

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In the past two decades the world has experienced an increase in the prevalence of type 2 diabetes. This is probably because of a marked decrease in daily physical activity combined with constant food abundance. However, our genome was probably selected from criteria that were characterized fluctuations between periods of feast and famine. The theory of thrifty genes states that these fluctuations are required for an optimal metabolic function.

In order to test this hypothesis we induced oscillation in the energy depots of 8 healthy young males (25±1 yr; BMI: 25.9±0.4 kg · m⁻²) by subjecting them to intermittent fasting every second day for 20 h for 15 days. Euglycaemic hyperinsulinemic (40 mU · min⁻¹ · m⁻²) clamps were performed after an overnight fast (8 hours) before and after the intervention period. The last 20 h fasting period was followed by 30 hrs normal eating before last overnight fast. Also, the subjects were instructed to eat the double amount of food as they normally would on days of non-fasting which resulted in maintained body weight (88.8±2.1 kg; coefficient of variation: 0.7±0.1%). Plasma FFA was unchanged after an overnight fast before and after the intervention (347±18 and 347±33 microM), whereas the FFA concentrations were 423±86, 652±98 and 574±77 microM in the end of the 2nd, 4th, and 6th fasting period, confirming that the subjects were indeed fasting. The concentration of plasma ketone bodies followed the pattern of FFA (0.10±0.04 mM after 20 hrs fasting vs. 0.06±0.02 after 8 hrs fasting).

Insulin mediated whole body glucose uptake rates increased from 6.3±0.7 to 7.3±0.5 mg · kg⁻¹ · min⁻¹ (P=0.03). This increase in insulin sensitivity was not accompanied by changes in fasting plasma glucose concentrations (5.1±0.1 vs. 5.0±0.1 mM). By the end of the 2nd, 4th, and 6th fasting period plasma adiponectin were increased compared to basal levels before the two clamps (5922±991 vs. 3860±784 ng/ml), whereas leptin was decreased (1344±244 vs. 2116±396 pg/ml). Plasma IL-6, TNF alpha as well as muscle glycogen and triglyceride did not change during the intervention.

This experiment is the first in humans to show that intermittent fasting, with oscillations in energy stores, increases insulin mediated glucose uptake rates. Furthermore, this study indicates that one of the mechanisms behind exercise training mediated increases in insulin action may be via repetitive oscillations in fuel stores. This view is compatible with the Thrifty gene concept.