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

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Introduction
In the past two decades the world has experienced an increase in the prevalence of type 2 diabetes. A main reason behind this is the lack of daily physical activity combined with food abundance. Our genome was probably selected in the Late Palaeolithic period (50,000-10,000 BC) from criteria that favored survival in a physical demanding environment like our ancestors hunter- and gatherer society. Fluctuation between feast and fasting was probably not unusual, resulting in oscillations in fuel stores, plasma insulin and metabolic regulatory proteins which in turn may have driven a selection of a metabolic genotype optimal for such conditions. The theory of thrifty genes states that these feast-famine cycles are required for an optimal metabolic function (Booth et al., 2002; NEEL, 1962).

Methods
8 healthy males were fasted every second day for 2 weeks giving a total of 7 fasting periods. Before and after euglycemic hyperinsulinemic clamps (40 mU x min-1 x kg-1) and microdialysis in the s.c. abdominal adipose tissue were performed after an overnight fast. After the last fasting period, subjects were allowed to eat for 30 h. Biopsies were taken in the m. vastus lateralis before and after the clamp at each occasion. During the fasting intervention blood samples were taken after the 2nd, 4th, and 6th day of fasting.

Results
Without any change in either body weight or % body fat (Table 1) the insulin mediated whole body glucose uptake rates increased from 6.3±0.1 to 7.3±0.5 mg kg⁻¹ min⁻¹ (P=0.03) (fig. 1). Additionally, the insulin mediated inhibition of lipolysis was increased after the fasting intervention, as determined by a larger drop in interstitial glycerol concentrations in the adipose tissue. 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). Plasma FFA was equal after an overnight fast before and after the intervention (347±18 and 347±33 microM), whereas it were increased to 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 opposite pattern of FFA being lower at the three days of testing (0.10±0.04 mM after 20 hrs fasting vs. 0.06±0.02 after 8 hrs fasting).

Discussion/Conclusion
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.

References

Table 1: Subject characteristics.

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<tr>
<th>N</th>
<th>Before</th>
<th>After</th>
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<tbody>
<tr>
<td>Age (y)</td>
<td>25±1</td>
<td>25±1</td>
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<tr>
<td>BMI (kg x m⁻²)</td>
<td>25.7±0.4</td>
<td>25.5±0.3</td>
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<td>% Body Fat</td>
<td>20.1±0.8</td>
<td>20.4±1.1</td>
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