A novel view of adipose tissue function: victim rather than cause of insulin resistance

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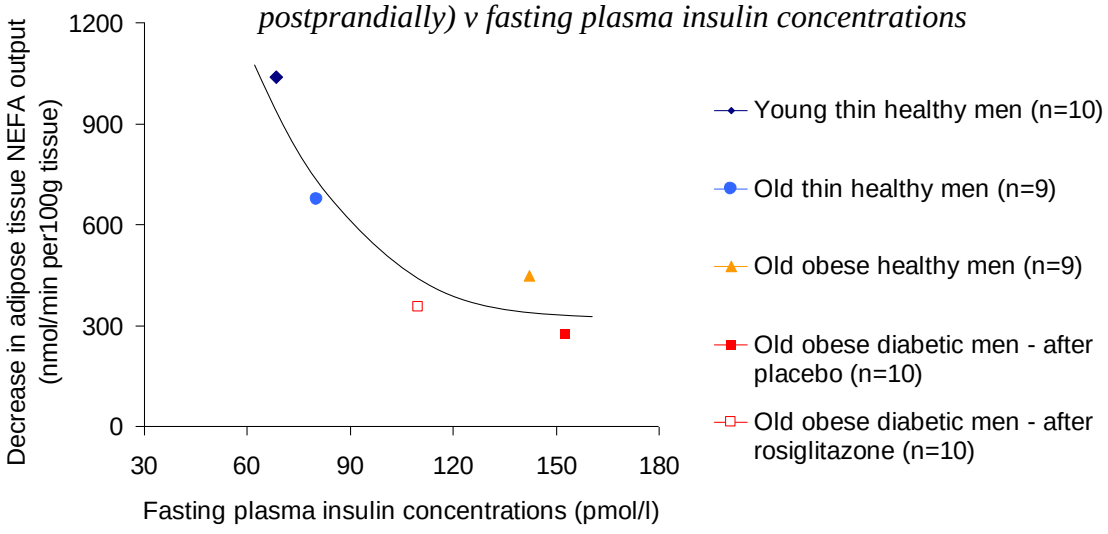
The regulation of non-esterified fatty acid (NEFA) release from adipose tissue (AT) is an insulin sensitive process. As insulin concentrations rise postprandially, AT NEFA release is suppressed. In insulin resistance, it is thought that AT does not suppress its NEFA release as much as in insulin sensitive individuals, a process leading to insulin resistance elsewhere in the body. We tested this widely accepted hypothesis.

We studied AT metabolism of four groups spanning a range of insulin sensitivity: *(i)* ten obese, diet-treated type 2 diabetic men after placebo and after rosiglitazone treatment; *(ii)* nine insulin resistant, non-diabetic men, age- and BMI-matched with group (i); *(iii)* nine lean insulin sensitive, non-diabetic men age-matched with group (ii); and *(iv)* ten young insulin sensitive, non-diabetic men, BMI-matched with group (iii). All groups underwent fasting and postprandial AT function assessment using measurements of blood flow and arteriovenous metabolite concentrations across subcutaneous abdominal AT.

As expected, all subjects decreased their AT NEFA release as plasma insulin concentrations increased postprandially. Plasma insulin was higher in insulin resistant subjects. Although postprandial suppression of AT NEFA release is an insulin sensitive process, surprisingly all groups suppressed their AT NEFA release (expressed per unit of AT mass) to the same level, irrespective of the degree of insulin resistance. Fasting AT NEFA output was expected to be higher in insulin resistant subjects, but in fact this was higher in insulin sensitive subjects. Thus, in insulin resistance, AT NEFA output per unit mass was largely suppressed in both the fed and fasting states. In contrast, insulin sensitive subjects modulated their AT NEFA output from fasting-to-fed states, although the systemic effect of this is influenced by total AT mass.

These data do not support the concept of insulin resistance in AT. Instead, AT merely responds to ambient insulin concentrations; the hallmark of insulin resistance's effect on AT is a loss of modulation of NEFA metabolism from fasting-to-fed states.

Figure: Decrease in adipose tissue NEFA output (from fasting to 120 minutes postprandially) v fasting plasma insulin concentrations



Funding: G.D.T. was funded by the Medical Research Council, and F.K. by the Wellcome Trust.