

# Overexpression of *Il6* leads to hyperinsulinaemia, liver inflammation and reduced body weight in mice

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## Abstract

**Aims/hypothesis** IL-6 is released by the adipose tissue and increased circulating levels in obesity are associated with hyperinsulinaemia and insulin resistance. Short-term experiments suggest that increased IL-6 release by the skeletal muscle following exercise may improve insulin sensitivity.

**Methods** In order to examine the effect of chronically elevated IL-6 levels, we overexpressed *Il6* in skeletal muscle in mice using an electro-transfer procedure.

**Results** Circulating IL-6 levels were increased and the animals rapidly lost both weight and body fat, but food intake was unchanged, which is consistent with the finding

that IL-6 increased energy expenditure. Insulin levels were inappropriately elevated and combined with hypoglycaemia in spite of reduced 2-deoxy-D-glucose uptake by skeletal muscle. Insulin-stimulated glucose uptake by skeletal muscles *ex vivo* was reduced, probably due to the decreased amounts of glucose transporter (GLUT)-4. Beta cell insulin content was increased, while apparent beta cell mass was unchanged. Circulating serum amyloid A cluster levels were increased tenfold due to a pronounced proinflammatory state in the liver with infiltration of inflammatory cells. However, no liver steatosis was found, which may be accounted for by concomitant AMP kinase activation.

**Conclusions/interpretation** Chronically elevated IL-6 levels lead to inappropriate hyperinsulinaemia, reduced body weight, impaired insulin-stimulated glucose uptake by the skeletal muscles and marked inflammation in the liver. Thus, the pleiotrophic effects of chronically elevated IL-6 levels preclude any obvious usefulness in treating obesity or its associated metabolic complications in man, despite the fact that weight reduction may be expected.

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## Abbreviations

AMPK AMP kinase  
CMV cytomegalovirus  
CoA coenzyme A  
2-DG 2-deoxy-D-[1-<sup>3</sup>H]glucose  
GFP green fluorescent protein  
GLUT glucose transporter  
PKB protein kinase B  
VO<sub>2</sub> oxygen consumption