GLP-1 secretion is regulated by IL-6 signalling: a randomised, placebo-controlled study.

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IL-6 is a cytokine with various effects on metabolism. In mice, IL-6 improved beta cell function and glucose homeostasis via upregulation of glucagon-like peptide 1 (GLP-1), and IL-6 release from muscle during exercise potentiated this beneficial increase in GLP-1. This study aimed to identify whether exercise-induced IL-6 has a similar effect in humans.; In a multicentre, double-blind clinical trial, we randomly assigned patients with type 2 diabetes or obesity to intravenous tocilizumab (an IL-6 receptor antagonist) 8ămg/kg every 4ăweeks, oral sitagliptin (a dipeptidyl peptidase-4 inhibitor) 100ămg daily or double placebos (a placebo saline infusion every 4ăweeks and a placebo pill once daily) during a 12ăweek training intervention. The primary endpoints were the difference in change of active GLP-1 response to an acute exercise bout and change in the AUC for the concentration-time curve of active GLP-1 during mixed meal tolerance tests at baseline and after the training intervention.; Nineteen patients were allocated to tocilizumab, 17 to sitagliptin and 16 to placebos. During the acute exercise bout active GLP-1 levels were 26% lower with tocilizumab (multiplicative effect: 0.74 [95% CI 0.56, 0.98], $p = 0.034$) and 53% higher with sitagliptin (1.53 [1.15, 2.03], $p = 0.004$) compared with placebo. After the 12ăweek training intervention, the active GLP-1 AUC with sitagliptin was about twofold that with placebo (2.03 [1.56, 2.62]; $p < 0.001$), while GLP-1 AUC values showed a small non-significant decrease of 13% at 4ăweeks after the last tocilizumab infusion (0.87 [0.67, 1.12]; $p = 0.261$).; IL-6 is implicated in the regulation of GLP-1 in humans. IL-6 receptor blockade lowered active GLP-1 levels in response to a meal and an acute exercise bout in a reversible manner, without lasting effects beyond IL-6 receptor blockade.; Clinicaltrials.gov NCT01073826.; Danish National Research Foundation. Danish Council for Independent Research. Novo Nordisk Foundation. Danish Centre for Strategic Research in Type 2 Diabetes. European Foundation for the Study of Diabetes. Swiss National Research Foundation.

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