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Moderate ethanol supply inhibits both glycogen synthesis and glycogenolysis in the perfused and isolated rat liver

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In isolated and perfused rat liver a positive glucose-dependent linear correlation between the net fluxes (Fn) of ATP and glycogen (Glg) has been found only in presence of insulin (Ins; Fn(Glg) = 72.5Fn(ATP) + 172); this result indicates that Ins can control the Glg store via energy metabolism[(1)]. Any change in this relationship in the presence of a substrate could then indicate a variation in insulin sensitivity. In the presence of a moderate ethanol (EtOH) supply (10 mM) the slope of the correlation is 4-fold higher (284.5Fn(ATP) + 2848), suggesting that for the same change in the consumption Fn of ATP Glg consumption is lower. Thus, the unidirectional hepatic fluxes (synthesis and lysis) of Glg were investigated in the presence of 10 mM-EtOH.

Male Wistar rats (100 g) were fasted for 48 h in order to deplete the liver Glg store. Livers were then perfused with an isotonic buffer (5 ml/min per g; 37°C; O_2–CO_2, 95 : 5 (v/v)) containing 30 mM-glucose (enriched with 20% [1-^{13}C]glucose) + Ins (120 mIU/l) + 2 mM-fructose to induce Glg synthesis. In a second step [^{13}C]glucose was replaced by 30 mM-glucose to investigate glycogenolysis. EtOH (10 mM) was added either in the Glg synthesis or the glycogenolysis phase (*n* 3 for each dataset). The change in the Glg content was monitored by ^{13}C NMR (Brucker DPX400, 9.4T; Brucker, Bremen, Germany); since ATP is consumed for Glg synthesis, its hepatic content was measured by ^{31}P NMR.

The 48 h fasting induced a dramatic decrease in liver Glg content (−99%). In the Glg synthesis study perfusion with [^{13}C]glucose + fructose induced an increase in the liver [^{13}C]Glg content (synthesis rate 2.4 (SE 0.2) μmol/h per g)), followed after 25 ± 5 min by a decreased rate (0.66 (SE 0.07) μmol/h per g; within 30 min). After the addition of EtOH at 25 min of the incorporation phase a plateau of [^{13}C]Glg content was observed, suggesting (a) inhibition of Glg synthesis or (b) an increase in glycogenolysis.

In the glycogenolysis study replacement of [^{13}C]glucose with 30 mM-glucose resulted in a decrease in [^{13}C]Glg (−0.69 (SE 0.08) μmol/h per g) indicating glycogenolysis. The subsequent addition of EtOH reduced glycogenolysis (−0.09 (SE 0.01) μmol/h per g).

A moderate EtOH supply in presence of Ins inhibits both hepatic Glg synthesis and glycogenolysis.

1. Baillet-Blanco L, Beauvieux MC, Gin H, Rigalleau V & Gallis JL (2005) *Nutr Metab* **2**, 32–41.