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Title: Intrauterine growth retardation (IUGR) promotes sensitivity to the satietogenic effect of palmitoleate in young rats.

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Intrauterine growth retardation (IUGR) due to perinatal malnutrition predisposes to obesity at adulthood. Animal studies have shown that IUGR alters the regulation of food intake (FI), increasing this risk of adult obesity. Short term regulation of FI relies on a functional nutrient sensing in the gut by entero-endocrine cells (EEC). Studies have demonstrated that long chain fatty acids such as oleate or palmitoleate initiate satiation via a mechanism that imply G-protein receptor (GPR) 40 or 120 expressed in cholecystokinin (CCK)-secreting EEC located at the upper intestine. We hypothesized that IUGR impacts the nutrient sensing in the gut which could lead to further alteration of the short-term regulation of FI.

The aim of the present study was to analyze nutrient sensing of long-chain fatty acids (palmitate and palmitoleate) known to stimulate the secretion of a major satiety peptide, cholecystokinin, by duodenal EEC and the gastrointestinal function (gastric motility, intestinal permeability,...) regulated by ENS, in 2 month-old IUGR rats obtained by protein restriction [8% (restricted, R) vs 20% (Control, C)] of their dams during gestation and lactation.

R rats weighted significantly lower (9%) than C rats but their relative FI measured 90min following 24-h fasting was similar. Orally administrated palmitate (500mg/kg) prior re-feeding had no effect on FI as compared to vehicle (polysorbate 80 1.5%) while palmitoleate (210mg/kg) significantly decreased (24%) FI in R rats compared to C group. This palmitoleate-induced reduction of FI in R rats may be related to the higher concentration of plasma CCK measured in this group. Both in vivo and ex vivo assessment of paracellular permeability using sulfonic acid conjugated with fluorescein showed that palmitoleate increased permeability in R rats compared to vehicle while there was no effect in C rats. Gastric contractile response induced by electrical field stimulation showed that palmitoleate blunt the response to L-Name and atropine in R rats only, suggesting an impact of IUGR on the contractile response to this satietogenic nutrient.

Our data show an increased sensitivity to the satietogenic effect of palmitoleate in juvenile IUGR rats. This unexpected response seems to be mediated by increased CCK secretion and duodenal permeability as well as a higher smooth muscle tone in the antrum of the stomach.