



Time window-dependent effect of perinatal maternal protein restriction on insulin sensitivity and energy substrate oxidation in adult male offspring

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Epidemiological and experimental evidence suggests that a suboptimal environment during perinatal life programs offspring susceptibility to the development of metabolic syndrome and Type 2 diabetes. We hypothesized that the lasting impact of perinatal protein deprivation on mitochondrial fuel oxidation and insulin sensitivity would depend on the time window of exposure. To improve our understanding of underlying mechanisms, an integrative approach was used, combining the assessment of insulin sensitivity and untargeted mass spectrometry-based metabolomics in the offspring. A hyperinsulinemic-euglycemic clamp was performed in adult male rats born from dams fed a low-protein diet during gestation and/or lactation, and subsequently exposed to a Western diet (WD) for 10 wk. Metabolomics was combined with targeted acylcarnitine profiling and analysis of liver gene expression to identify markers of adaptation to WD that influence the phenotype outcome evaluated by body composition analysis. At adulthood, offspring of protein-restricted dams had impaired insulin secretion when fed a standard diet. Moreover, rats who demonstrated catch-up growth at weaning displayed higher gluconeogenesis and branched-chain amino acid catabolism, and lower fatty acid β -oxidation compared with control rats. Postweaning exposure of intrauterine growth restriction-born rats to a WD exacerbated incomplete fatty acid β -oxidation and excess fat deposition. Control offspring nursed by protein-restricted mothers showed peculiar low-fat accretion through adulthood and preserved insulin sensitivity even after WD-exposure. Altogether, our findings suggest a testable hypothesis about how maternal diet might influence metabolic outcomes (insulin sensitivity) in the next generation such as mitochondrial overload and/or substrate oxidation inflexibility dependent on the time window of perinatal dietary manipulation.

Résumé en anglais

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