EXPERIMENTAL MODELS FOR STUDYING PERINATAL LIPID METABOLISM

Long-term effects of perinatal undernutrition

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Abstract: By using different experimental designs in the rat we have been able to answer several unanswered questions on the short- and long-term effects of alterations of lipid metabolism during the perinatal stage. The first was to demonstrate the importance of maternal body fat accumulation during the first half of pregnancy, since undernutrition in this critical period when fetal growth is slow, impedes fat depot accumulation and not only restrains intrauterine development but has long-term consequences, as shown by an impaired glucose tolerance when adults. Secondly, undernutrition during suckling has major long-term effect of decreasing body weight, even though food intake is kept normal from the weaning period. Our findings also show that a diet rich in n-3 fatty acids during pregnancy and lactation has adverse effects on offspring development, but cross fostered experiments showed that this effect was a consequence of the intake of these fatty acids during the lactation period rather than during pregnancy. Pups from dams that were fed a fish oil-rich diet during pregnancy and lactation were found to have altered glucose/insulin relationship at the age of 10 weeks. Since a n-3 fatty acid-rich diet decreases milk yield during lactation, additional experiments were carried out to determine whether decreased food intake or altered dietary fatty acid composition, or both, were responsible for the long-term effects on the glucose/insulin axis.

Results show that the decreased food intake caused by a n-3 fatty acid-rich diet rather than the change in milk composition during suckling was responsible for the reduced pancreatic glucose responsiveness to insulin release at 16 weeks of age.

In conclusion, present findings indicate that impaired maternal fat accumulation during early pregnancy and food intake during lactation, rather than a difference in dietary fatty acid composition, have major effects on postnatal development and affect glucose/insulin relationships in adult rats.
1. INTRODUCTION

Impaired fetal and early postnatal growth confers an increased susceptibility for the development of adult chronic disease such as type 2 diabetes, obesity and cardiovascular disease (3; 15). Early nutrition influences development and can cause adaptive and permanent changes in structure, physiology and metabolism (14). During pregnancy, the availability of nutrients to the foetus depends on those crossing the placenta from maternal circulation, which depends on maternal nutrition. In order to determine how changes in maternal nutrition during pregnancy and lactation have short- and long-term consequences on offspring development and susceptibility for causing adult disease, appropriate experimental models are needed, due to ethical and methodological limitations. By using the rat, we applied different experimental designs to study the effects of alterations in maternal nutrition during the perinatal stage on lipid metabolism, and its consequences on postnatal development and susceptibility to alter the glucose/insulin relationships.

2. SHORT- AND LONG-TERM EFFECTS OF MATERNAL UNDERNUTRITION DURING THE FIRST HALF OF PREGNANCY

During pregnancy, the concept of maternal nutrition must be extended beyond a mother’s diet to include her body composition and metabolism (6). Lipid metabolism plays a major role in maternal metabolic adaptations to warrant the availability of substrates to the foetus (7; 8). The accumulation of fat depots in maternal tissues is a constant characteristic feature in pregnancy (11; 19; 20), and takes place mainly during the first half of gestation, when opposite to the insulin resistant condition that occurs during late pregnancy, there is even an enhanced sensitivity of adipose tissue to insulin (17). A decrease in the capacity of the mother to accumulate fat depots during this early part of