Impacts of prenatal malnutrition and an early obesogenic diet on adipose tissue morphology and gene expression

Sharmila Ahmad[1], Lise K. Lyngman[1], Rajan Dhakal[1], Morteza Mansouryar[1], Mohammad Moradi[3], Prabhat Khanal[2] and Mette O. Nielsen[1]

[1]Section for Production, Nutrition and Health,
Department of Veterinary and Animal Sciences (IVH), University of Copenhagen
[2]Department of Nutrition, Lipid Droplets Research Group,
Norwegian Transgenic Centre (NTS), University of Oslo
[3]Department of Animal Science, Sari Agricultural Science and Natural Resources University (SANRU), Iran

Introduction: Adipose tissues in precocial species develop and differentiate during mid-late gestation, which makes their postnatal function sensitive to in utero nutrient restriction. Nutrition insults, in the form of under- as well as overnutrition, during this period can have long term implications for adipose tissue structure and metabolism of the offspring later in life. In the present study, we aimed to investigate whether 1) phenotypic manifestations in adulthood of such a prenatal programming on adipose tissue structure and function al traits (gene expression) can be affected by the nutrition exposure in early postnatal life, and 2) whether dietary correction later in life can reverse the long-term consequences of early life malnutrition.

Materials and methods: A total of 36 twin bearing cross-bred Texel ewes (last 6 weeks of pregnancy, term=147 days) were fed NORM (100% energy and protein), HIGH (150% energy and 110% protein) or LOW (50% NORM) diet. Postnatally, twin lambs were subjected to a conventional (CONV) or an obesogenic high-starch-high-fat (HCHF) diet from days 3 until 6 months of age. A subgroup of animals (not slaughtered at 6 months of age) were thereafter fed the same conventional diet until 2½ years of age and then humanely euthanized. Adipose tissue from different depots was used for histological evaluation and determination of expression of a range of genes.

Results:

Subcutaneous adipose tissue

Females exposed to prenatal malnutrition and/or fed an early postnatal obesogenic diet (except for LOW-CONV) had a higher proportion of larger adipocytes (6400-25600µm2) compared to CONV females that were adequately nourished in fetal life. A similar shift was observed in CONV-HCHF compared to NORM-CONV males. The results are consistent with the gene expression analysis, where a lower expression was found for genes involved in adipogenesis and angiogenesis in the prenatal malnourished groups, which may compromise subcutaneous adipocyte hyperplasic growth, hence predisposing for hypertrophic growth and consequently adipocyte enlargement.

Mesenteric adipose tissue

Undernourished females had the highest percentages of large adipocytes (12800-25600µm2=16.09% and 25600-36000µm2=2.39 %) than males. In males, prenatal under- (LOW) and overnutrition (HIGH) shifted the distribution of adipocyte size in the direction of larger adipocytes with an area between 12800 to 36000µm2. However there were no effects of neither prenatal nor postnatal nutrition exposures on gene expression in mesenteric adipose tissue, except for PPARγ and FAB4.

Perirenal adipose tissue

Individuals exposed to prenatal malnutrition and early postnatal obesogenic diet had increased proportion of larger (6400-12800 µm2) adipocytes compared to NORM-CONV sheep. Analysis of gene expression revealed that HSL and IL6 genes were up-regulated in undernourished groups, while VEGF, IL6 and MCP1 genes were down-regulated in the groups malnourished pre- or postnatally compared to

NORM-CONV. However, the morphological changes in adipocytes were apparently not related to expression of the studied genes.

Epicardial adipose tissue

Both males and females had an increased proportion of larger adipocytes (6400 to 128000μm2) when they had been exposed to the early postnatal obesogenic diet. Furthermore, up-regulation of lipid metabolism and adipogenic genes was also found in the HCHF groups. This indicates that the early postnatal HCHF diet targeted epicardial adipose tissue with permanent implications in adulthood.

Conclusion: Subcutaneous and perirenal, but not mesenteric and epicardial, adipose tissues were targets of fetal programming with long-term implications for structure and gene expression, which were expressed in LOW irrespective of the postnatal diet, but surprisingly in HIGH mostly upon exposure to the mismatching CONV diet. Implications of early obesity development were not reversed by dietary correction later in life, and were expressed mostly in pericardial tissue. Pre- and/or early postnatal malnutrition predisposes for (presumably less healthy) hypertrophic rather than hyperplasic growth, and males appeared to attain a more female-like phenotype upon exposure to malnutrition in early life.