Maternal food-restriction leads to a drastic downregulation of H4K16 acetylation in IUGR rat placentas

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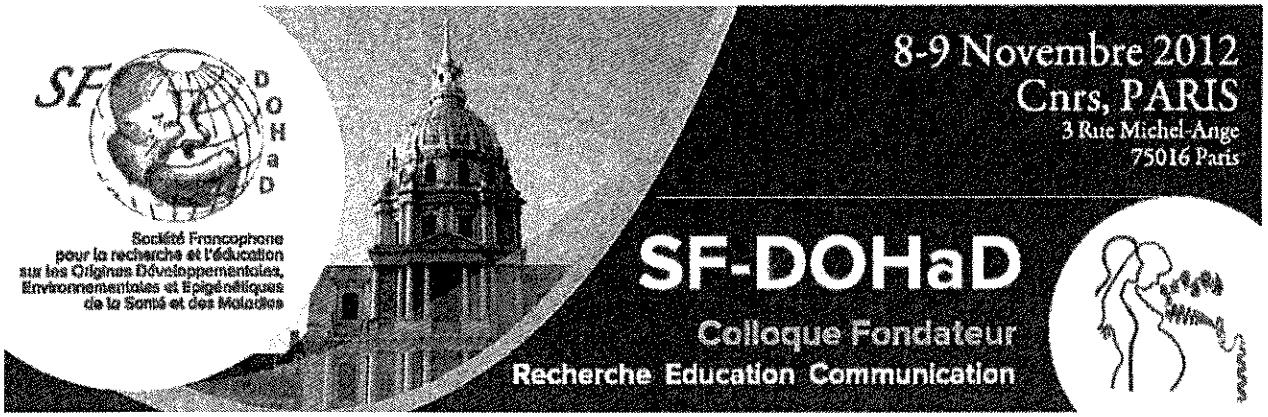

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now recognized as one of the factors contributing to the developmental programming of chronic diseases in later life.[2,3] To date, there is no relevant animal model that displays impaired glucose tolerance without diabetes during gestation to investigate the mechanisms underlying fetal overgrowth in pregnancy complicated with MGH. We have developed a rat model and investigated the effects of maternal dysglycemia on fetal growth and placental gene expression. Female rats were injected with nicotinamide and streptozotocin (N-STZ) 1 week before mating. N-STZ treatment induced impaired glucose tolerance in late gestation, resulting in metabolic disorders and fetal overgrowth in more than 20% of newborns. Placental mass was also increased in N-STZ macrosomic pups compared with normotrophes, and associated with a rise in the labyrinthine zone. Gene and protein expression of lipoprotein lipase was increased in N-STZ placentas from macrosomic pups. We reported that expression of insulin receptor and glucose transporters genes was down-regulated in macrosomic placentas, whereas the expression of amino acid transporters was not modified. For the first time, we showed that insulin-like growth factors and nutrient transporter genes were also differentially expressed in the placentas from normal pregnancies when the number of fetuses within the litter varies. The N-STZ model offers the potential for further studies into the effects of MGH on placental function that will allow better understanding of the mechanisms underlying fetal overgrowth. We propose that the regulation of placental gene expression constitutes a mechanism of physiological adaptation that is taking part during late gestation to optimize fetal growth and assure the viability at birth when the number or the size of fetuses is inappropriate.

Key words: animal, fetal growth, gestational diabetes, placenta

Statement of interest: Authors report no conflict of interest.

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POSTER N°37

Characterization of the placental development in the intrauterine growth-retarded piglet

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In pig production, the selection of hyperprolific animals has lead to an increased rate of intrauterine growth-retarded piglets in litters. Intrauterine growth retardation (IUGR) is an important economic issue inducing a higher mortality rate, a lower growth capacity, a higher muscular lipid content in carcasses and less tender meat. The maternal and fetal environments interact through the placenta to maintain nutrient supply of the fetus. The aim of this work was to explore placental adaptive mechanisms throughout pregnancy in IUGR piglets. Possible changes in placental morphometry and gene expression of the IUGR piglet were prospected, using a natural IUGR pig model. Placental samples from 18 pairs of control (normal birth weight) and IUGR fetuses at gestation days (gd) 45, 71 and 112 were analyzed by stereology. The expression of 10 candidate genes potentially associated with placental development and IUGR was examined by RT-qPCR. The DNA methylation of the insulin-like growth factor 2 (IGF2) imprinting gene was evaluated by pyrosequencing. Glycemia and fructosemia were measured in IUGR and control fetuses at gd 71 and 112. No morphometric abnormality was found in the IUGR placenta. An increased expression of the IGF2 gene, however, was observed in the IUGR chorionic tissue at gd 71 ($\times 1.48$, $P < 0.05$). No difference was shown, however, in the DNA methylation levels of the IGF2 gene. Fructosemia was significantly reduced in IUGR fetuses at gd 71, but not at gd 112, whereas glycemia remained normal at both stages. IGF2 affects the placental growth and the placental permeability by modulating the nutrient transport levels. This increase could be a compensatory mechanism from the placenta to meet the fetal nutrient demand and maintain fetal growth at mid-gestation. Indeed, there was a tendency for the expression of glucose transporter GLUT3 to be reduced at gd 71.

Key words: critical periods, fetal growth, large animals, placenta, pregnancy

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POSTER N°45

Maternal food-restriction leads to a drastic downregulation of H4K16 acetylation in IUGR rat placentas

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Undernutrition during gestation is associated with an increased susceptibility to metabolic and cardiovascular diseases. Placenta, as a widely recognized programming agent, contributes to the underlying processes. Alterations in both placental development and activity are well known to constitute programming events for offspring's physiology and metabolism in adulthood. Growing experimental evidences suggest that epigenetic marks may serve as a memory of exposure to inappropriate environments and thus could be implicated in foetal programming.[1] Our aim was to explore whether maternal undernutrition could disturb epigenetic processes in the placenta of intrauterine growth-restricted (IUGR) foetuses. Two experimental IUGR models were used: pregnant Wistar rats were subjected to a 70% food restriction along the gestation (FR30 model);[2] or to a 50% food restriction during the last week of gestation (FR50).[3] We investigated the global level of four epigenetic marks in full-term placentas. DNA methylation was assessed using LUMA and performed western blot assays for H3K9me3, H3K4me3 and H4K16ac, three important histone marks.[4] We did not observe any change in H3K9me3, H3K4me3 and DNA methylation, but a decrease in placental H4K16ac, in both models and in both sexes. High-performance liquid chromatography/high-performance capillary electrophoresis quantified the decrease of H4 monoacetylation: −12% in FR30 males, −18% in FR50 males and −22% in FR30 and FR50 females. As both models were similarly affected, our findings suggest that the last third of gestation may be a critical period for H4K16ac set-up in placenta. This epigenetic mark may constitute a nutritional sensitive target during foetal programming and may be an important link between nutrition and epigenetic programming during foeto-placental development.

Key words: epigenetics, IUGR, placenta, programming

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FOOD PREFERENCES, EATING BEHAVIOUR AND COGNITIVE DEVELOPMENT

3 – A. Chango and C. Delpierre

Studies in the session suggest a prenatal role of maternal PUFA consumption on child psychomotor development. Stress is reported to promote palatable food intake and highlight the critical role of early nutrition in neurodevelopment and behavioral responses later in life. Malnutrition during early life sensitizes the offspring to the development of metabolic and neurological disorders in adulthood. Data indicate that, in addition to induce stable epigenetic modifications in the hippocampus, perinatal malnutrition alters the plastic epigenetic responses underlying learning and memory.

ORAL N°24

Early nutrition: impact on the development of food preferences and eating behavior

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Early nutritional status not only affects health on the long term but it also affects food preferences and eating behavior at different stages in the developing child. Moreover, eating behavior in early childhood tracks until adulthood.[1] Modes of feeding evolve in the first years of life, starting from cord feeding, going through a transitional phase of milk feeding to ultimately end by eating the family diet. These transitions involve a series of adaptations, which will ultimately affect food preferences, eating behavior and, as a result, weight and health status. Understanding the development of eating behavior in the current context of a wide availability of palatable foods is therefore central to address key societal issues such as the epidemics of obesity and to provide parents with science-based feeding recommendations. This presentation aims at showing the impact of breastfeeding and of practices of complementary feeding on eating behavior in the 1st year of life. Maternal milk bears flavors from the foods ingested by the mother and its tastes different from that of formula milk: it will be shown how breastfeeding affects the infant's food preferences around the time of complementary feeding, as shown by experimental studies in human infants and by a longitudinal study.[2,3] At this age, infants display varied reactions toward new foods according to the sensory properties of the foods.[4] Moreover, based on results from varied experimental studies, it will be shown how complementary feeding practices, in particular introduction of a variety of foods, affect further food acceptance.[4]

Key words: early life nutrition, human, infant feeding/breastfeeding

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