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Nutritional status before and during pregnancy in relation to the maternal insulin-like growth factor-system and health related variables in the offspring

Studies in women, guinea pigs and rats

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Akademisk avhandling

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ABSTRACT

Adequate fetal growth is of importance for health in adulthood. Maternal nutritional status has been suggested to be one major factor influencing fetal development. The nature of how the mother's nutritional status and her metabolic, endocrine and physiological adaptations to pregnancy interact and how these interactions affect fetal growth is unclear. The insulin-like growth factor (IGF)-system has been suggested to be one mediator between maternal nutritional status and fetal growth. Impaired fetal growth may have life-long effects, but little is known about the possibilities to ameliorate intrauterine perturbations postnatally. Oxytocin, an anti-stress hormone, was used as a model to study such possibilities.

The aims were: to measure serum levels of IGF-I, IGF-II, IGF-binding protein (IGFBP)-1, IGFBP-3 and protease activity against IGFBP-3 in healthy women before, during and after pregnancy; to study the relationships regarding maternal body weight and composition before and during pregnancy versus components of the maternal IGF-system in serum in healthy women; to study the relationships regarding components of the maternal IGF-system in serum versus infant birth weight; to measure the expression of mRNA for IGF-I and IGF-II in different tissues in guinea pigs and to study how these expressions are altered by gestation and food restriction; to study long-term effects of maternal food restriction during gestation on health related variables in adult rat offspring; to study long-term effects of early postnatal treatment of oxytocin in the adult rat offspring.

Healthy women were studied before pregnancy, in weeks 8, 14, 20, 32, 35 of pregnancy and 2 weeks post partum. Body weight, body composition and serum levels of IGF-I, IGF-II, IGFBP-1, IGFBP-3 and protease activity against IGFBP-3 were measured. Infant body weight and length at birth were obtained from hospital records. The amounts of mRNA for IGF-I and IGF-II in the liver, adipose tissues, muscles, spleen, uterus and placenta were measured in virginal and pregnant guinea pigs, being either ad libitum fed or food restricted. Rat dams were either ad libitum fed or food restricted during gestation. Their offspring received oxytocin or NaCl at day 1-14 of age. Blood pressure, plasma levels of corticosterone, IGF-I, IGFBP-1, and reproductive performance were measured in the adult offspring.

All of the studied components of the IGF-system in serum underwent changes during pregnancy. The levels of IGF-I were reduced in early pregnancy compared to before conception. The lower the body weight or the less amount of body fat before pregnancy, the larger the decrease in IGF-I in early pregnancy. The combination of body weight before pregnancy and the serum level of IGF-I in early pregnancy explained as much as 47 % of the variation in birth weight, indicating that the higher the maternal body weight before pregnancy and the lower the level of IGF-I in early pregnancy, the heavier the infant. From week 20 of pregnancy, maternal levels of IGFBP-1 were negatively correlated to birth weight. In late pregnancy, the abundance of IGFBP-1 and protease activity in serum together explained 35 % of the variation in birth weight, indicating that the lower the IGFBP-1 and the higher the protease activity, the higher the birth weight. In guinea pigs, mRNA for IGF-I was expressed in high amounts in adipose tissue and liver, whereas mRNA for IGF-II were highly expressed in placenta and liver. The expression of IGF-I was in general unaffected by food restriction, but doubled during gestation, whereas the expression of IGF-II in the placenta was decreased by food restriction and increased in the liver by gestation. Maternal food restriction during gestation caused increased levels of corticosterone, IGF-I and IGFBP-1, but no elevation in blood pressure, in adult offspring. Early postnatal oxytocin treatment decreased blood pressure and corticosterone, whereas the influence on reproductive performance was dependent on the nutritional status of their dams and the current nutritional experience in adulthood.

In conclusion, this thesis confirms that the IGF-system may be one factor mediating the effects of maternal nutritional status on fetal growth. It also supports the suggestion that IGFBP-1 in maternal serum may be used as a marker of infant birth weight. Adipose tissue was shown to produce high amounts of IGF-I, indicating endocrine functions during gestation. Postnatal oxytocin treatment ameliorated some of the adverse effects in adult offspring, induced by maternal food restriction.

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