Nutritional peculiarities during the prenatal period and physical status of the offspring: a pilot experimental study

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Nutrition in uterus has a significant influence on the formation of metabolic phenotype in offspring generations. The objective of this study was to investigate maternal nutrition and the changes in body weight at few generations of rat offspring.

Materials and methods. 12 maternal rats and 121 offspring rats were used in the study. Mature female Wistar rats were divided into 3 groups with respect to nutritional restriction (one control and two experimental groups). Rats from the first experimental group (1 EG) were 50 percent food-restricted one month prior and during the pregnancy; rats from the second experimental group (2 EG) were 50 percent food-restricted exclusively one month prior to the pregnancy. After weaning all the pups were fed with control diet, weighted weekly, observed and evaluated for the morphological indices of metabolic stress.

Results and conclusions. Maternal nutritional restriction in pre-pregnancy and pregnancy may alter the physical status and behaviour of the offspring: the reactions differ in both sexes; the alterations depend on the time window of exposure. There were no weight-related differences between groups in body weight of female offspring rats during the all time periods of the study. The first generation 1 EG male offsprings were the heaviest; the tendency for a greater than control group weight was also observed at the second generation up till the early reproductive period. The 2nd generation 2 EG male rats were the heaviest and exhibited some evident markers of chronic diseases.

Key words: nutritional deprivation, pregnancy, growth programming, thrifty phenotype

INTRODUCTION

The pathogenesis of chronic diseases depends not only on the environmental factors of the adult individual, but also on the critical moments during his / her growth and development, particularly on the period in uterus, also on the conditions before pregnancy (1). Global slimming trends, especially at the post-communistic countries, and prevailing promotion of a slender or even exhausted woman’s body often lead to dissatisfaction with one’s
appearance and trigger efforts to lose weight (2). Some human studies and data on animal research showed the link between insufficient nutrition before pregnancy or at the time of pregnancy, and child’s susceptibility to various health problems (3–19). The studies often describe various hormonal, cardiovascular, behavioural changes, as well as catch-up growth as a result of prenatal growth retardation. The lack of nutrients in uterus causes the formation of “thrifty phenotype”, which means that the body is “programmed” to act in a sustainable mode, thus giving an advantage to survive under conditions of nutritional deprivation (20, 21).

Scientific knowledge regarding dietary restriction and further pregnancy outcomes as well as the risk for health is under discussion. In most cases, the studies that provide data on the consequences of prenatal starvation are based on hypothetical theories and retrospective studies. Hence, there is a specific need in prospective studies with laboratory animals to test the above mentioned theories. In addition, this issue is almost unexamined in the context of aging and survivability. Moreover, the prevalence of abnormal metabolic parameters in several offspring generations is purely studied.

The objective of this study was to investigate maternal nutrition (the dietary conditions before and during pregnancy) and the changes in body weight as well as the risk for obesity at few rat offspring generations from birth up till natural death.

MATERIALS AND METHODS

The animals were housed under standard conditions in the Vivarium of the Institute of Biochemistry. All animal procedures were in accordance with the State Food and Veterinary Service (Permit No. 0211). The cohort of 12 mature female Wistar rats was divided into 3 groups with respect to nutritional restriction. The rats were fed either a normal (control group) or restricted diet: one experimental group was food-restricted one month prior to and through the pregnancy period (1 EG) and the other was food-restricted one month prior to pregnancy only (2 EG). Food-restricted rat groups received 50 percent less of the feed eaten in the control group. The maternal rats and the offspring rats were mated at the age of 3–4 months. Body weight was measured weekly with the same calibrated scales starting at the age of 1–1.5 months. Maternal rats were euthanized after weaning. Both offspring generations were kept and weighted under the same standardized conditions. We also evaluated offspring rat’s appearance, behaviour (the interest in the environment, fear, aggression, nervousness), and other signs of metabolic stress.

Differences between the groups were compared using the one-way analysis of variance (ANOVA) followed by the LSD test; p < 0.05 was considered statistically significant.

RESULTS

We did not find weight-related differences between 1 EG and 2 EG female offspring rats during the entire study period – both at the first and the second generations of offspring (Figs. 2, 4 respectively). The first generation 1 EG male offspring rats were the heaviest from 3 months of age (Fig. 1); the tendency for a bigger than control group weight was also observed at the 2nd generation up till the early reproductive period (Fig. 3). In the first offspring generation, pre-pregnancy food deprived male rats (2 EG) had similar weight to that of the control group (Fig. 1). However, 2 EG were the heaviest at the second offspring generation starting from the fourth month of age with few minor exceptions (Fig. 3).

DISCUSSION

Nutrition in uterus has a significant influence on the formation of metabolic phenotype in offspring generations. Our study did not find weight differences in food deprived female offspring rats. Scarce literature data complements our results (12, 13). It is estimated that female’s organism is more adaptive and therefore is able to compensate the stress induced by food restriction (11–15).

Prenatal metabolic stress might also induce “catch up” growth, and the body weight of food deprived offspring rats increases faster than control offspring’s weight. Other studies find similar results to those of our study: food deprived male offspring rats weighted more than other control and experimental rats (11–13). In addition, the increase in weight continues even after the catch-up is reached,
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**Fig. 1.** Weight dynamics in the first generation of male offspring rats

**Fig. 2.** Weight dynamics in the first generation of female offspring rats

**Fig. 3.** Weight dynamics in the second generation of male offspring rats
and the subsequent weight increase is due mostly to the fat mass increment (3, 16, 18, 19, 22).

The nutrition exclusively before pregnancy is an almost unexamined topic in the context of offspring health later in the individual’s life. It is hypothesized that good physical condition of the mother could partially balance the altered metabolism induced by the nutritional deprivation (23–26). Pre-pregnancy food deprived males were the heaviest as well as demonstrated the majority of the evident external pathology in the second offspring generation. We hypothesize that these offspring rats got the energy saving phenotype from their starved mothers, however, after birth the nutritional conditions for the offspring rats changed, and the “re-programming” might have occurred.

Few animal studies described altered changes in adipose tissue topography, insulin and leptin metabolism even in the case if no weight related differences between groups were observed (3, 11–14, 27–29). Our study did not examine biochemical indices as well as body fat deposition (although the evident central fat distribution was observed in aged male rats from experimental groups in comparison with control ones). Exclusively in the experimental groups, we also followed the morphological indices of the metabolic stress. We have recorded some behavioural disorders such as nervousness, aggressiveness and the opposite – sluggishness, poor spatial orientation and reaction to stimuli. Behavioural pathologies are frequently described in the context of relationship between mother’s food deprivation and health risk of her offspring (30–32). In addition, these symptoms were evident at a relatively early age and more common in males than females. We have also observed a number of external indices of stress such as red tears, neck and face oedema, hair loss and others that are considered an important marker for the rodent health risk (33). However, we did not find the similar studies concerning these symptoms. Furthermore, dissection after spontaneous death showed a number of health problems in the experimental groups: tumours, necrotic changes in regulatory organs (heart, liver, lungs, brain) as well as enlargement of hypophysis (an indicator of premature aging). As mentioned, the second generation pre-pregnancy food deprived male rats not only were the heaviest, but also exhibited the majority of the mentioned pathologies. Since the lifespan research with animals is rare, we could not find similar studies regarding the mentioned changes found in autopsy as well as other deleterious effects of epigenetically influenced aging.

Growth programming is a much more complicated process than it was considered up till yet, and frequently its consequences cannot be foreseen. In some cases our study complements other findings, but we have also received a few unexpected results (particularly differences between two experimental groups). The complex epigenetic changes related to nutritional deprivation and their influence on growth and aging remain unclear. The underlying mechanisms as well as the effects of maternal food deprivation in pre-pregnancy and pregnancy should be investigated further.

![Fig. 4. Weight dynamics in the second generation of female offspring rats](image-url)
CONCLUSIONS

Maternal nutritional restriction during and before pregnancy may alter the physical status and behaviour of the offspring: the reactions differ between sexes and depend on the time window of exposure. This pilot study shows the necessity for further investigations of larger samples of the experimental groups.

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References


