

Perinatal High-fat Diets Induce Hepatic Steatosis in Rat Offspring, which is fully Reversible and do not Induce Liver Ceramide Accumulation.

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Objective: The objectives of present study were: 1) To determine if hepatic steatosis in rat-pups, induced by high-fat feeding of the dams during pregnancy and lactation leads to increased accumulation of ceramide in the young rat-liver and if the steatotic-state is reversible after transfer to low-fat diets.

Methods: Female Sprague-Dawley rats were fed *ad libitum* one of two experimental diets, for 10 days before pregnancy, during pregnancy and during suckling. The diets were chow containing 5 % fat (w/w) (C) or chow with added palm oil (total fat content 23 % (w/w)) (HF diet). At 48 hours postpartum, litters were reduced to 8 pups. Twenty days *post partum*, one male pup from each litter was sacrificed. The remaining male pups from each litter were split into 2 groups after weaning (21days *post partum*). Half of the offspring from dams fed the control diet continued on this diet (C→C) while the other half were fed the HF diet (C→HF). The offspring from the dams fed the HF diet was splitted in the same way (HF→C and HF→HF). After 70 days *post partum*, one male offspring from each litter were again sacrificed. Food intake and weight gain were analyzed daily and lipids were analyzed with standard methods.

Results: Total energy intake was identical between the groups, both in the dams pre-weaning and in the pups post-weaning. At 20 days of age, pups from the HF mother suffered from severe hepatic steatosis with TAG concentration of 43 ± 11 mg/g compared to 12 ± 5.2 mg/g in the C-group ($p < 0.0001$). Despite the very high liver TAG levels in the HF-group, there was no difference in the ceramide content of the livers; average ceramide levels being approximately 90 nmol/g. However, at 70 days of age (after 50 days on the post-weaning diets), the pups from the HF mothers that were given the control diet post-weaning had as low TAG levels as the C→C pups (6.6 ± 1.5 and 6.2 ± 1.3 mg/g, respectively). On the other hand, pups raised by dams on the control diet, that had been switched to the high fat diet (C→HF) had increased TAG levels as had the HF→HF pups (21 ± 8.5 and 24 ± 6.9 mg/g, respectively). Interestingly, at the age of 70 days, hepatic ceramide concentration was significantly higher in the two groups that had been given HF-diets, compared to the post-weaning control groups (C→HF 106 ± 19 & HF→HF 102 ± 15 nmol/g vs. C→C 82 ± 4.4 & HF→C 84 ± 12).

Conclusion: Although energy intake was identical in C and HF dams, pups from the HF dams developed hepatic steatosis. However, in the lactating pup, this did not lead to increased hepatic ceramide levels, whereas high-fat feeding after weaning caused increased ceramide accumulation in the liver. High-fat feeding of the dams during pregnancy and lactation did not have any programming effect, since no effect of the pre-weaning diets was observed in either liver TAG or ceramide at 70 days of age.