Abstract: 42O

Characterising brain inflammation during pregnancy in a new mouse model of metabolic syndrome

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The prevalence of metabolic syndrome (MetS) is increasing at alarming rates. The brain undergoes striking changes in both MetS and pregnancy. While it is well-recognised that MetS increases the risk of maternal and fetal complications in pregnancy, the effect of MetS on maternal and fetal brain inflammation is poorly understood. Therefore, this study aimed to characterise maternal and fetal brain inflammation in a mouse model of MetS. Female C57BL/6 mice were placed on high-fat diet (42% kcal in food) with high sugar and salt in their drinking water (10% high fructose corn syrup and 0.9% NaCl; HFSS) or normal chow diet (NCD) at 5 weeks of age (n=18-19 per diet) for 10 weeks. Following this, females were mated with male C57BL/6 mice for conception. Female mice were mated up to three times, and the mice that did not successfully get pregnant were studied as non-pregnant mice. Bodyweight, blood pressure, and fasted blood glucose status were measured regularly throughout the diet-regimen pre- and post-conception. Mice were culled at endpoint (18.5 days following conception in pregnant and age-matched timepoints in non-pregnant mice), and fetal and maternal brains were processed for flow cytometry. In both non-pregnant and pregnant mice, HFSS significantly ($P < 0.01$) increased body weight, fasting blood glucose and blood cholesterol. Flow cytometry revealed that HFSS significantly ($P = 0.04$) reduced overall leukocyte counts within the maternal brain. Specifically, overall T cells (CD3+) and cytotoxic T cells (CD8+) were reduced in the brains of pregnant mice ($P = 0.0098$ and $P = 0.0346$, respectively), but not in those of non-pregnant mice. HFSS did not affect any of the assessed leukocyte populations in fetal brains. Of note, all studied T cell populations (CD3+) were negligible (<10 cells detected) within the fetal brain, suggesting that at gestational day 18.5, cerebral T cells are not yet developed. Overall, this study suggests that metabolic disturbances prior to pregnancy promote brain inflammation in pregnant mothers but not in their pups. Moreover, cerebral leukocyte populations were not affected by HFSS in age-matched non-pregnant mice, suggesting that the brain is particularly susceptible to the effects of MetS during pregnancy. We are currently completing histopathology and qPCR studies to better understand the physiological consequences of reduced cerebral T cells during pregnancy in MetS mice.