8 Effect of prenatal methyl donor enriched diet on fetal programming of adult blood pressure

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OBJECTIVE: Epigenetic modifications through DNA methylation and histone acetylation are known to affect gene function, and have been implicated in fetal programming of adult diseases. As a methyl donor, folate is known to affect these epigenetic modifications. We hypothesized that prenatal folate supplementation will prevent the altered fetal programming of adult blood pressure in a previously characterized transgenic animal model of utero-placental insufficiency induced by lack of endothelial nitric oxide.

STUDY DESIGN: Homozygous NOS3 knockout (KO) and wild type mice (WT) were cross-bred to produce maternally- (KOM, n=8) and paternally-derived (KOP n=10) heterozygous male offspring. During pregnancy the dams were allocated either a methyl' donor enriched diet (MDD, NIH31, 15mg folic acid) or regular chow. The dams were allowed to deliver, and their diet as well as that of the offspring was switched to regular chow. At 14 weeks of age, blood pressure (BP) was measured in the unrestrained offspring by telemetry. BP catheters were inserted through the left carotid artery into the aortic arch and BP was recorded continuously for 7 days. Mean (MBP), systolic (SBP) and diastolic (DBP) BP were averaged over 12 hour periods. One-way ANOVA was used for statistical analysis ($p<0.05$ denotes significance).

RESULTS: There was no difference in KOM and KOP pup number between mothers that received MDD or regular diet. Pup weight was similar at 14 weeks of life between the 2 groups. In offspring from the control diet group, BP in the KOM was significantly higher than KOP. Prenatal MDD diet significantly decreased BP in both KOM and KOP offspring. The percent change in diastolic and mean BP was not significantly different between KOM and KOP, but the MDD effect on the systolic BP was significantly more pronounced in the KOP (figure).

CONCLUSIONS: Prenatal administration of diet rich in methyl donor partially reverses the effect of uterine environment on altered programming of adult blood pressure. Epigenetic modifications play a role in the fetal origin of adult diseases. Supported by NHLBI 3R01HL080558-04S1