Hyperlipidemia and glucose intolerance at late maturity following neonatal hypoxia in rats

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INTRODUCTION: There is increasing evidence of early life stress leading to Metabolic syndrome at maturity. Metabolic syndrome is an aggregation of risk factors (overweight, abdominal obesity, hypertension, dyslipidaemia and glucose intolerance) that strongly correlates with cardiovascular disease. We have previously shown that neonatal hypoxia is associated with an increase in arterial blood pressure in male rats that persists to late maturity. The aim of this study was to investigate the effects of hypoxia for the first ten days of life on the lipid profile and glucose tolerance at late maturity in male rats.

METHODS: Experiments were conducted on adult male Sprague-Dawley rats aged 8 months. An experimental group (n=8) was raised in hypoxia (FiO2 = 0.12) for the first ten days of life and subsequently raised in normoxia (Neonatal Hypoxia). A second group (n=13) was reared in normoxia without exposure to hypoxia (Control). At 8 months rats from each group were fasted overnight. Venous blood was obtained for measurement of triglycerides, cholesterol and HDL. A glucose tolerance test was performed (0.5g/kg glucose i.v.) with venous sampling of glucose at 1, 5, 10, 15, 20, 30 minutes and the area under the glucose response curve calculated for each animal. Two-tailed, unpaired t-tests were performed (P<0.05). All data are presented as mean ± SEM.

RESULTS: Fasting serum triglycerides, cholesterol and HDL were significantly elevated in the 8 month old neonatally hypoxic rats compared to controls (3.01±0.73 vs. 0.94±0.15, 2.84±0.59 vs. 1.52±0.07, 1.95±0.32 vs. 1.39±0.06 mmol/l). The response to the glucose challenge was also significantly impaired in the neonatally hypoxic rats compared to controls (area under the curve 151±18 vs. 233±32).

CONCLUSION: Our results indicate that neonatal exposure to hypoxia in the rat is associated with hyperlipidemia and glucose intolerance at late maturity. Together with our findings of increased arterial pressure this suggests the possibility of neonatal programming of adult Metabolic syndrome by early life hypoxia. This raises the question of long-term cardiovascular risk factors incurred by hypoxemia in early life in adult survivors of cyanotic congenital heart disease unrelated to surgical repair or residual cardiac defects.

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