



IUGR AMPLIFIES ATHEROSCLEROSIS AND INSULIN RESISTANCE IN RATS FED A HIGH FAT DIET

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Intrauterine growth restriction (IUGR) refers to the condition of a fetus or newborn being unable to reach their growth potential due to development in a less than optimal *in utero* environment. Globally, most women eat a high fat diet (HFD) during pregnancy, so IUGR most often occurs in mothers consuming an HFD. However, the mechanism of how the combination of a maternal HFD and IUGR cause insulin resistance and cardiovascular disease is relatively unknown. The association was examined through a rat model, created by Dr. Zinkhan's lab, combining IUGR and maternal HFD. The rat model variables included high-fat or regular diet, IUGR or non-IUGR, and male or female. Multiple combinations were made using the dietary variables in both the diet of the parent generation as well as their offspring.

The insulin responsive glucose transporter 4 (Glut4) plays a key role in regulating glucose homeostasis in insulin sensitive tissues, including liver, muscle, and adipose tissue. We hypothesized that Glut4 membrane translocation was decreased in the liver, muscle, and adipose tissue of the IUGR-HFD rats injected with insulin. Preliminary results through glucose testing show baseline fasting Glut4 protein was decreased in the non-physiological fat (liver, visceral adipose, and muscle) storage depots of IUGR-HFD rats, as well as significantly higher fasting blood glucose levels in these rats. This highlights the increased insulin resistance in IUGR-HFD rats, and that IUGR may increase lipid accumulation in non-physiologic tissues resulting in higher risks of cardiovascular disease.

Therefore, we also hypothesized that IUGR offspring exposed to a maternal HFD and weaned to an HFD would be more likely to have abnormal fat accumulation in their tissues. Oil Red O (ORO) staining of the aorta, muscle and liver tissue samples was used to measure abnormal lipid deposits induced by IUGR and a maternal HFD in rats. An increased amount of fat in a sample is indicative of the perinatal environment inducing an abnormal uptake or storage of fat in non-physiologic storage depots in the muscle and liver, as well as the development of atherosclerosis in the aorta. When fed an HFD, male control and IUGR rats had the same muscle and liver lipid staining, but female control rats had more lipid staining than IUGR rats. IUGR male and female rats had more and larger fatty streak lesions in the aorta. This suggests the IUGR-HFD rats are more likely to have atherosclerosis, therefore increasing the risk of myocardial infarction, stroke, and death, than non-IUGR rats on the same HFD, highlighting the importance of the prenatal environment in adult cardiovascular disease.