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"Metabolic Effects of High-Fat Diet in Female Mice"

Background: High-fat diets (HFD) have become increasingly prevalent in contemporary times, prompting concerns regarding their impact on metabolic health. These diets are associated with issues such as impaired glucose tolerance, insulin resistance, and obesity, all of which can evolve into metabolic syndrome and cardiovascular diseases. Our preliminary study showed that when female mice on HFD were bred with regular diet (RD)-fed males, a significant portion of their pups died for unknown reasons, raising questions about the broader implications of HFD on metabolic and reproductive health as well as offspring viability. This study explores how a HFD affects metabolism, especially glucose and insulin function, in female mice preconception.

Methods: An intraperitoneal glucose tolerance test (ipGTT) and intraperitoneal insulin tolerance test (ipITT) were conducted on twenty C57BL/6J female mice, with ten on RD (22 kcal% fat) and ten on HFD (60 kcal% fat), at 10 and 11 weeks into their diets, respectively. While the mice were fasting for five hours, the volume of 25% glucose or 0.1 U/mL insulin were prepared based on each mouse's body weight, with the final dosage being 2 g/kg glucose and 0.5 U/kg insulin. After the fasting period, baseline fasting blood glucose levels were obtained (Time 0) by puncturing the tail vein and measuring with OneTouch glucose meters and test strips. Subsequently, the glucose/insulin solution was injected directly into the peritoneal cavity. Blood glucose concentrations (mg/dL) were then measured at 15, 30, 60, 90, and 120 minutes, with values recorded and any irregularities noted.

Results: The ipGTT data revealed a statistically significant difference in blood glucose concentrations between the RD and HFD groups at all time points ($p<0.05$). While both peaking around 30 minutes, the HFD group had a significantly larger magnitude of elevation than the RD (389.2 vs. 211.6 mg/dL, p=6.3E-0.6). At 120 minutes, the HFD group had a significantly larger difference from baseline compared to the RD group (110.5 vs. 38.4 mg/dL, $p=0.00024$). In other words, the HFD group had significantly elevated glucose levels at its peak and returned to its baseline less quickly than the RD group. Similar to ipGTT, ipITT data showed that HFD group had a statistically significant higher blood glucose concentrations at all time points ($p<0.05$). Importantly, the HFD group had a statistically significant less reduction in blood glucose as a percent change after insulin administration at 15, 30, and 60 minutes than the RD group.

Conclusion: The results indicate that chronic consumption of HFD lead to metabolic dysfunction in the female mice, specifically impaired glucose tolerance and insulin resistance. The next step of the current study is to mate these female mice on RD and HFD with RD-fed males. The ipGTT and ipITT will be performed on the mothers postpartum, as well as on the offspring, to better understand the broader implications of HFD on maternal health and potential impact on offspring.