Metabolic Effects of High-Fat Diet on Female Mice

Christine Tseng[1], Lucyna Wojcik[2], Nour Abbes[3], Dr. Xinping Yue[3]

[1]Haynes Academy for Advanced Studies, [2]Isidore Newman School, [3]LSUHSC Cardiovascular Center of Excellence

Introduction

- High-fat diets (HFD) are becoming increasingly common, raising concerns about their impact on metabolic health.
- These diets are associated with impaired glucose tolerance, insulin resistance, and obesity, which in turn heighten the risk of metabolic syndrome and cardiovascular diseases.
- In our previous preliminary study, pups born to female mice on a HFD and males on a regular diet (RD) experienced a higher level of mortality.
- This raises important questions about the broader implications of HFD on metabolic and reproductive health as well as the viability of offspring.

Research Objective

This study aims to investigate the impact of a HFD on metabolic processes, with a particular focus on glucose regulation and insulin sensitivity in female mice during the preconception period.

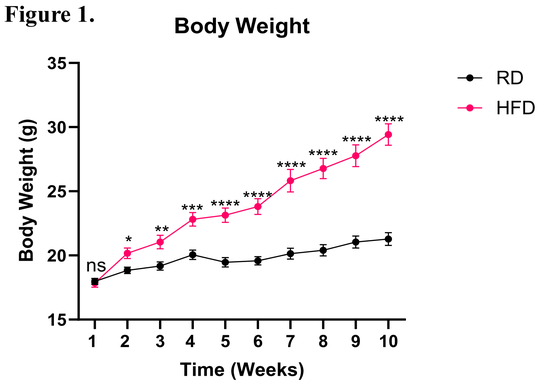
Experimental Design

Twenty female C57BL/6J mice, 6 weeks old, were assigned to diets:

- 10 on a high-fat diet (HFD, 60 kcal% fat)
- 10 on a regular diet (RD, 22 kcal% fat)

with 5 per cage. They have been on these diets for 10 weeks and counting now (**Figure 1**).

Figure 1.



Methods

- An intraperitoneal glucose tolerance test (ipGTT) and intraperitoneal insulin tolerance test (ipITT) were conducted on these female mice at 10 and 11 weeks, respectively.
- During the five-hour fast, solutions of 25% glucose and 0.1 U/mL insulin were prepared based on the mice's body weight, with dosages of 2 g/kg glucose and 0.5 U/kg insulin.
- Baseline fasting blood glucose levels were measured by puncturing the tail vein using OneTouch glucose meters and test strips (Time 0).

- Subsequently, the glucose/insulin solution was injected directly into the peritoneal cavity.
- Blood glucose levels (mg/dL) were then recorded at 15, 30, 60, 90, and 120 minutes, with any irregularities noted.

Results

Figure 2a.

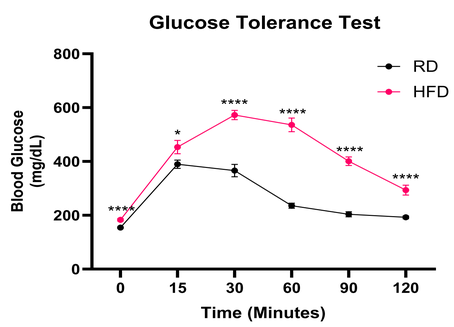


Figure 2b.

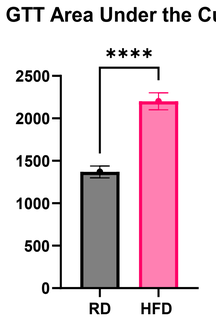


Figure 3a.

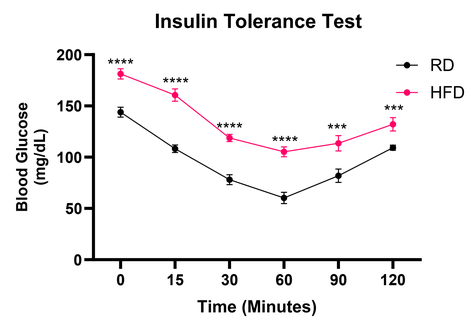


Figure 3b.

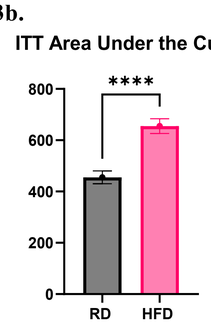


Figure 3c.

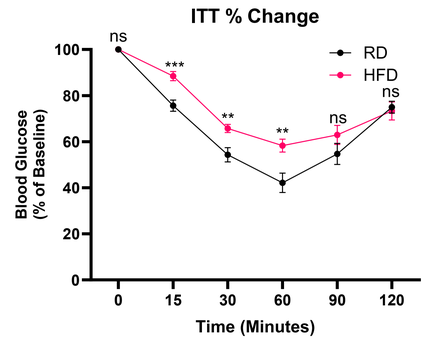
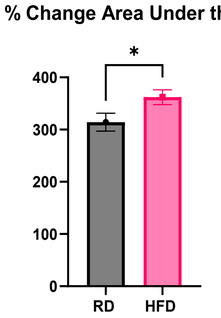


Figure 3d.



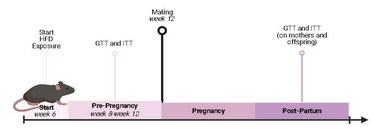
Key

ns: $p \geq 0.05$ (Not Significant)
*: $p < 0.05$ (Significant)
**: $p < 0.01$ (Very Significant)
***: $p < 0.001$ (Very Significant)
****: $p < 0.0001$ (Extremely Significant)

- The ipGTT data revealed a statistically significant difference in blood glucose levels between the RD and HFD groups at all time points (**Figure 2a**).
- The HFD group showed a significantly higher Area Under the Curve (AUC) than the RD group (2201 vs. 1369, $p < 0.0001$), indicating impaired glucose tolerance (**Figure 2b**).
- Similarly, the ipITT data revealed that the HFD group had significantly higher blood glucose levels at all time points (**Figure 3a**) and a greater AUC (654.8 vs. 455.1 ,$p < 0.0001$), indicating insulin resistance (**Figure 3b**).
- Notably, the HFD group showed a significantly smaller change in blood glucose reduction after insulin administration at 15, 30, and 60 minutes compared to the RD group (**Figure 3c**).
- The HFD group also had a significantly higher AUC (362.1 vs. 314.3, $p<0.05$), indicating impaired insulin sensitivity (**Figure 3d**).

Conclusions and Future Directions

- The results indicate that chronic consumption of HFD leads to metabolic dysfunction, specifically impaired glucose tolerance and insulin resistance, in female mice.
- 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.



References

- Harmancıoğlu, B., & Kabaran, S. (2023, May 10). Maternal high fat diets: impacts on offspring obesity and epigenetic hypothalamic programming. *Frontiers in Genetics*, *14*. PubMed Central. https://doi.org/10.3389/fgene.2023.1158089
- Whitehead, A. K., Li, Z., LaPenna, K. B., Abbes, N., Sharp, T. E., Lefer, D. J., Lazartigues, E., & Yue, X. (2024, January). Cardiovascular dysfunction induced by combined exposure to nicotine inhalation and high-fat diet. *American Journal of Physiology*, *326*(1), H278-H290. Pub Med Central. https://doi.org/10.1152/ajpheart.00474.2023

This research project was supported through the LSU Health Sciences Center, School of Medicine.