The Impact of Sex and Diet on the Development of Metabolic Syndrome

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ABSTRACT

There are many different diets that may contribute to the development of metabolic syndrome. Metabolic syndrome is a cluster of conditions that increase a person's risk of cardiovascular disease. One aspect of metabolic syndrome is insulin resistance, which affects 7.3% of males and 6.6% of adult females. Muscle comprises 40% of the average body mass and helps to control insulin sensitivity. The purpose of this experiment was to determine how different diets alter the progression of insulin resistance in males compared to females. Mice were fed one of three diets control (20% fat, 20% protein, and 60% carbohydrates (18% sucrose)), High Fat (45% fat, 20% protein, and 35% carbohydrates (18% sucrose)), or high sugar (60% carbohydrates (100% sucrose), 20% protein, and 20% fat. Glucose tolerance test was conducted at 0 weeks, 6 weeks, and 11 weeks. Fasting insulin was measured in a subset of animals at weeks 6 and 12, and HOMA-IR was calculated. RNA was isolated from the skeletal muscle and RT-PCR was run for *Glut4* and *Igf1* genes. The male high fat diet group at 12 weeks had higher insulin, blood glucose, and HOMA-IR compared to all other groups. HOMA-IR was elevated in the HF males at 6wks, while no change was seen in the HS or female groups. There was no difference in gene expression of *Glut4* and *Igf1*. Conclusion: This data suggest that females may be protected from insulin resistance regardless of diet, and it may be regulated independently of muscle *Glut4* and *Igf1* expression.

INTRODUCTION

Metabolic syndrome is a cluster of conditions that increase a person's risk of heart disease. One of the more common conditions is insulin resistance. Insulin resistance is becoming a major problem in the world and the numbers continue to rise. It is believed that 7 out of every 1000 person in the US has diabetes or is prediabetic. This number has slowly been increasing since the 90's.[1] Glucose is one of the body's main sources of energy. The hormone insulin controls the amount of glucose that is circulating in the blood. Insulin circulates in the bloodstream, enabling sugar to enter your cells. Insulin resistance is when cells are not as responsive to inulin and therefore there is excess glucose circulating in the body. This is problematic and can cause serious complications such as cardiovascular disease, coma, and death. There are many factors that can influence the blood glucose in one's body: their diet, genetics, sex, environment, their overall health, sedentary lifestyle. Sex differences has become one of the focal points in trying to pinpoint why a person develops insulin resistance. According to the National Diabetes Report, written by the CDC, 7.3% of men and 6.6% of women who are 18 and older have been diagnosed type two diabetes. Other studies show rates in males ranging from 6%-21% while corresponding rates in females were 3.6-13.8% depending on the ethnicity.[2] According to this data, men are more likely to become insulin resistant than women are. We also looked at *Glut 4* and *Igf1* mRNA expression to see if there was a change in muscle signaling. These genes play a role in insulin sensitivity. In this experiment, we will be trying to determine if there is a difference in the progression of insulin resistance in males compared to females. Secondly, we will be looking at if diet impacts the onset of insulin resistance differently in males and females.

EXPERIMENTAL DESIGN

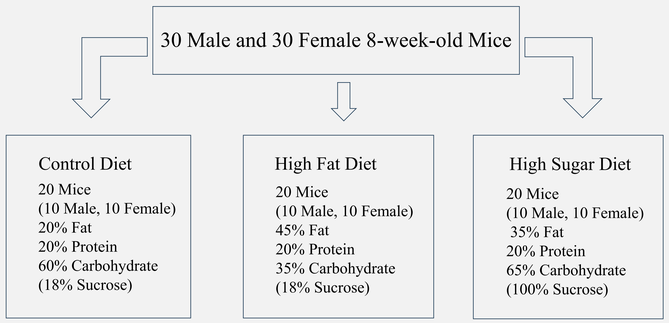
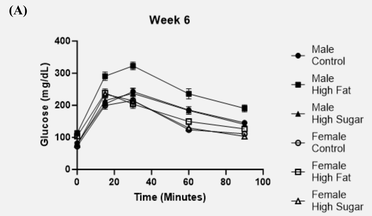
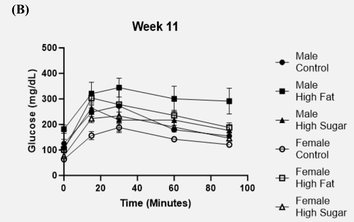


Figure 1. **Experimental design.** Glucose tolerance Test (GTT) was conducted monthly over the 12-week span on all mice to test fasting glucose and glucose levels after an intraperitoneal injection of glucose. Mice were fasted for 12 hours prior to GTT being conducted. Body weights were taken weekly. Half of the mice were sacrificed at 6-weeks; second half sacrificed a 12-weeks.

RESULTS

Figure 2. A) Body weight of the mice over the 12 –week span. All data are represented as mean ± SEM. Data were analyzed by two-way repeated measures ANOVA *significance was set at p<0.05.





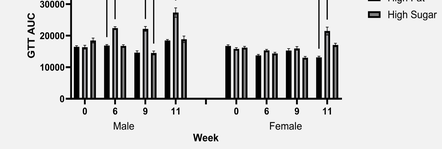
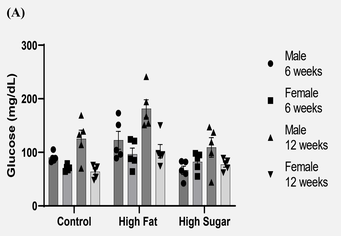
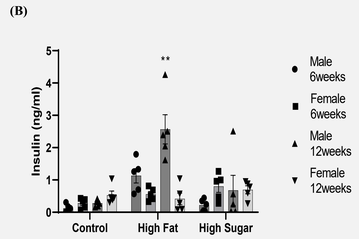


Figure 5 (A) 6-week glucose tolerance test measurement. (B) 11-week glucose tolerance test measurement. (C) The area under the curve of glucose tolerance tests at baseline, 6, 9, and 11 weeks. All data are represented as mean ± SEM. Data were analyzed by two-way ANOVA *significance was set at p<0.05.





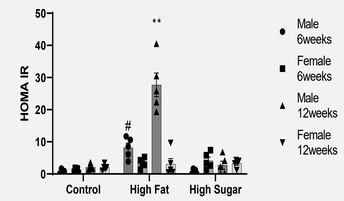
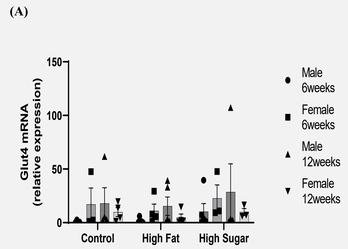


Figure 4. (A) Fasting blood glucose. (B) Fasting blood Insulin data collected from the ELISA from 6 weeks and 12 weeks. (C) HOMA IR calculated. ** Significant from all other comparisons. All data are represented as mean ± SEM. Data were analyzed by two-way ANOVA *significance was set at p<0.05.

RESULTS



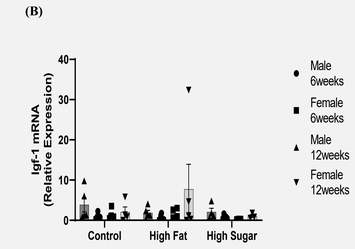


Figure 3. (A) *Glut4* gene expression and (B) *Igf1* gene expression in gastrocnemius muscle. All data are represented as mean ± SEM. Data were analyzed by two-way ANOVA *significance was set at p<0.05.

CONCLUSIONS

- Males on a high fat diet gained more weight compared to males on a high sugar diet and females on a high fat or high sugar diet
- Males consuming high fat diet became insulin resistant by 6 weeks as females did not become insulin resistant until week 12
- Despite showing systemic insulin resistance there was no change in muscle gene expression of *Glut4* and *Igf1*

FUTURE DIRECTIONS

- Additional markers of metabolic syndrome will be measured such as plasma triglycerides
- Function and location of GLUT4 protein in skeletal muscle will allow for analysis of glucose import into the cell as a marker of glucose intolerance

REFERENCES

1. National Diabetes Statistics Report." *Centers for Disease Control and Prevention*, Centers for Disease Control and Prevention, 29 June 2022, https://www.cdc.gov/diabetes/data/statistics-report/index.html.

2. Huebschmann, Amy G., et al. "Sex Differences in the Burden of Type 2 Diabetes and Cardiovascular Risk across the Life Course - Diabetologia." *SpringerLink*, Springer Berlin Heidelberg, 27 Aug. 2019, https://link.springer.com/article/10.1007/s00125-019-4939-5.