



At least 6.9 million Americans aged 65 and above are living with Alzheimer's disease (AD) as of 2024, and that number is only expected to increase as the aging population grows. The exact cause of AD has yet to be discovered, but there are several significant risk factors such as sleep deprivation, a lack of exercise, and diet quality. Our lab has investigated diet quality in relation to AD pathology through the creation of two representative diets, the Typical American Diet (TAD) and the Mediterranean Diet (MD). These diets are calorically matched and are used to investigate their long- and short-term effects on Alzheimer's pathology in C57BL/6J mice. To follow up on a previous study that used 6 months of diet exposure to explore the longer-term effects of these diets, groups of mice were fed either the TAD or MD for 3 months, beginning at 4 months of age, to better understand the short-term effects. This project then conducted histological analysis on the colon, liver, and gonadal white adipose tissue using different histological techniques. Specifically, a cryostat and microtome were used to prepare the tissue samples, and they were stained using Hematoxylin and eosin (H&E) staining and Oil Red O. Samples were then examined using confocal microscopy, and tissues from each diet were compared and analysed. We found that 3 months of diet led to excess hepatic lipid deposition, as was found in the 6-month study. Additionally, the 6-month study suggested that the TAD may have induced an insulin resistance (IR) state, so gonadal white adipose tissue was examined to explore adipocyte expansion after 3 months on diet. Preliminary colon histology was conducted to begin the exploration into gut dysbiosis and inflammation and the connection to Alzheimer's pathology. This study presents novel histological evidence of the impact of diet quality on peripheral tissue in relation to Alzheimer's disease.



### Methods

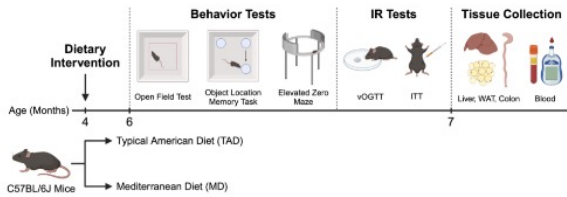


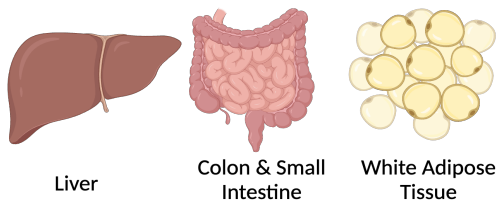
Figure 1. Study Timeline.

Table 1. Typical American diet and Mediterranean diet nutritional compositions.

	TAD			MD		
	grams%	kcal%	grams	grams%	kcal%	grams
<b>Carbohydrates</b>	53.7	50.0	495.5	48.0	50.0	495.3
<b>Protein</b>	16.0	15.0	147.3	14.3	15.0	147.2
<b>Fat (Total)</b>	16.6	35.0	153.1	14.8	35.0	153.2
<b>SFA</b>		17.0	74.4		6.7	29.5
<b>MUFA</b>		12.3	54.0		19.6	86.2
<b>PUFA</b>		3.2	14.1		5.6	24.4
<b>Insoluble Fiber</b>	5.4		50.0	8.3		85.4
<b>Soluble Fiber</b>				5.8		59.4

Table 2. Typical American diet and Mediterranean diet key ingredients.

	TAD	MD
<b>Carbohydrates</b>	Corn starch	Brown rice, wheat starch
<b>Protein</b>	Casein	Egg whites, fish, soy
<b>Fat</b>	Safflower oil, beef fat, butter	Olive, fish, and flaxseed oil
<b>Insoluble Fiber</b>	Cellulose	Cellulose
<b>Soluble Fiber</b>		Psyllium, inulin



### Liver Histology

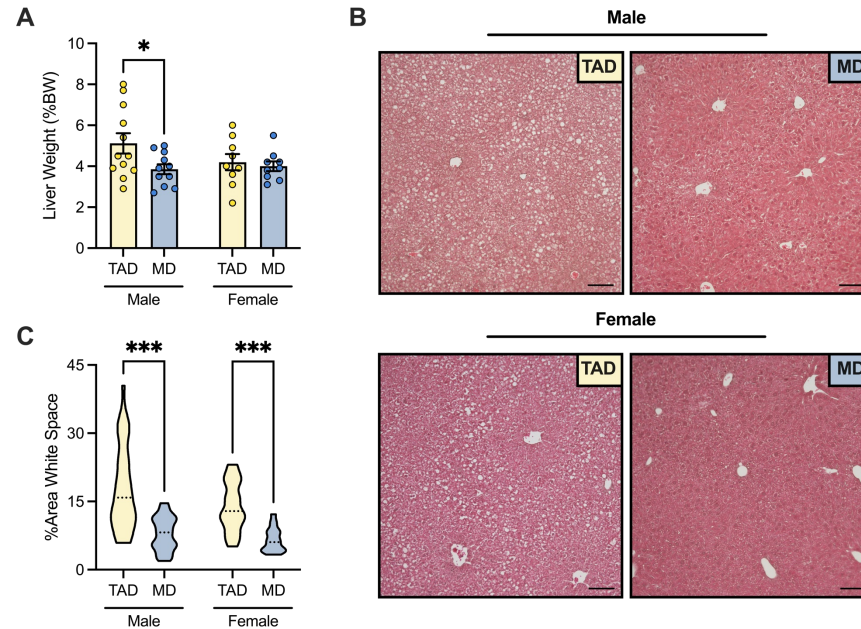
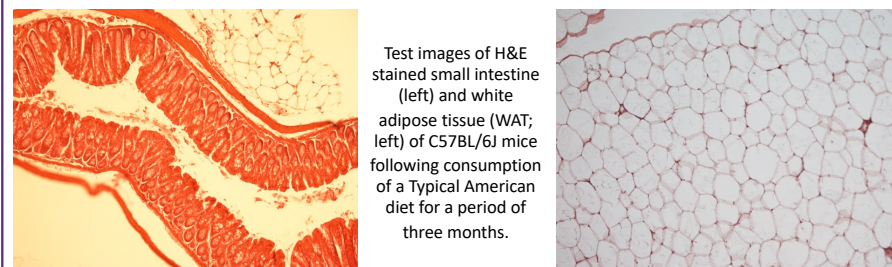


Figure 2. Increased hepatic lipid deposition in both males and females on the TAD.

### Preliminary Small Intestine & Adipose Tissue Histology



Test images of H&E stained small intestine (left) and white adipose tissue (WAT; left) of C57BL/6J mice following consumption of a Typical American diet for a period of three months.

### Conclusions

- We found striking evidence that consuming a Typical American diet over just a three-month period leads to increased lipid deposits in the liver.
- Though early in the analysis, there is some evidence suggesting that the consumption of the same Typical American diet over the course of three months leads to an increase in adipocyte size and altered intestinal morphology compared to consumption of a Mediterranean diet.

### Future Directions

- Continue analysis of white adipose (WAT) tissue to investigate differences in adipocyte morphology between a Typical American diet and a Mediterranean diet.
- Refines protocols for colon and small intestine histology to further explore the effects of diet on intestinal microvilli morphology and functionality.
- Replicate these findings in all three tissues of interest after a six-month diet consumption period to compare against our current findings.

### References

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