Exploring the Potential, Therapeutic Effects of the Mediterranean Diet on the Liver-Brain Axis in C57BL/6J Mice

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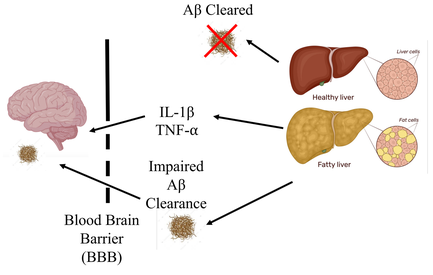
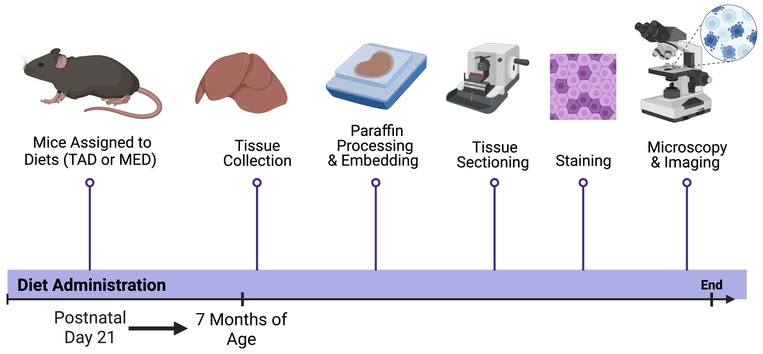
Alzheimer's Disease (AD) affects approximately 6.5 million Americans, and there is currently no cure. Prior research has shown that a key hallmark of AD is amyloid beta (Aβ), a protein that aggregates and forms plaques in the brain under pathological conditions. If Aβ is not cleared by the body, resultant plaques may disrupt proper cognitive and neuronal function (Więckowska-Gacek, 2021). As the liver plays a crucial role clearing Aβ, liver damage may jeopardize the efficacy of the liver to clear amyloid beta in the periphery of the body, enabling it to reach the brain. One way liver function can be disrupted is through diet, specifically the Typical American Diet (TAD). The TAD has been shown to cause non-alcoholic fatty liver disease (NAFLD) and inflammation, both of which are associated with AD. A TAD is classified as one that contains high amounts of refined sugars and saturated fats derived from animals (Lian, 2020). Conversely, the Mediterranean Diet (MD), a largely plant-based diet, contains high amounts of monounsaturated fatty acids and polyunsaturated fatty acids. These dietary factors have been shown to decrease inflammation and increase antioxidant effects, further protecting the brain from AD pathology (Castellanos-Tapia, 2020). Therefore, we hypothesize that the MD could protect the liver and be used as a potential prevention strategy for NAFLD and AD. The current study examined the effects of TAD and MD on the relationship between the liver and the brain in wild-type mice. During tissue collection, livers were taken and histologically analyzed. The livers from each experimental group were processed, stained, and evaluated for their overall composition.

Introduction



Key Dietary Components	Mediterranean Diet	Typical American Diet
Carbohydrate Sources	Brown rice & wheat starch	Corn starch
Fiber Sources	Cellulose, psyllium, inulin	Cellulose
Fat Sources	Olive oil, fish oil & flaxseed oil	Safflower oil, beef fat & butter
Protein Sources	Egg whites, soy & fish protein	Casein (from milk fat)

Methods



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Results

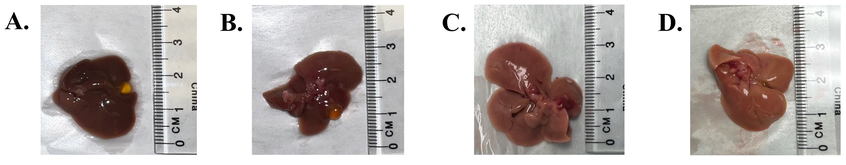

Figure 1. Whole isolated livers **A.** Male mouse fed the MD **B.** Female mouse fed the MD **C.** Male mouse fed the TAD **D.** Female mouse fed the TAD

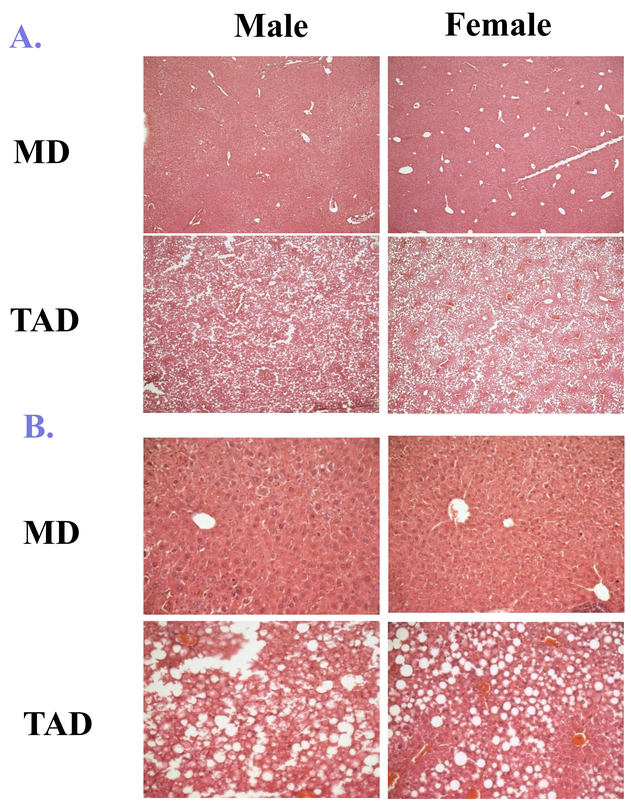

Figure 2. Histological liver sections from male and female mice on the Mediterranean diet (MD) or Typical American Diet (TAD); stained using Hematoxylin and Eosin. **A.** Magnification 4X **B.** Magnification 20X

Results

Figure 3. Histological liver sections from male and female mice on the MD diet stained using Oil Red O and Hematoxylin.

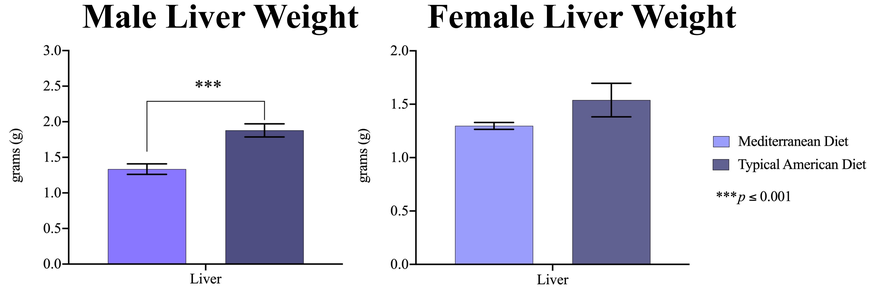

Figure 4. An independent samples t-test revealed a significant difference in liver weight ($p \leq 0.001$) following six months of diet. Bars represent mean ± SEM. n's = 10.

Figure 5. An independent samples t-test revealed that a difference in liver weight was approaching significance, ($p \leq 0.09$). Bars represent mean ± SEM. n's = 6–9

Conclusion

- Long-term consumption of TAD resulted in higher levels of fat deposition in the liver compared to the MD, as seen in the images taken from isolated livers and microscopy images.
- Livers from male mice on the TAD weighed significantly more due to the increased fat deposition

Future Directions

- In future studies, we will use Oil Red O staining to highlight and identify adipose cells within the liver.
- The liver is important for the clearance of Aβ from the periphery of the body, however, this function is disrupted due to fat deposition in the liver. Pathologies like NAFLD impair the liver's function of Aβ clearance from the periphery which can lead to damage of the blood brain barrier (BBB). This provokes the deposition of Aβ in the brain, which is common in neurodegenerative diseases, such as AD (Vegas-Suárez, 2022).

References

Castellanos-Tapia, L., Tejero-Barrera, M. E., Salas-Silva, S., Simoni-Nieves, A., Escobedo-Calvario, A., & Gomez-Quiroz, L. E. (2020). Mediterranean-like mix of fatty acids induces cellular protection on lipid-overloaded hepatocytes from western diet fed mice. *Annals of Hepatology, 19*(5), 489-496. https://doi.org/https://doi.org/10.1016/j.aohep.2020.06.005

Lian CY, Zhai ZZ, Li ZF, Wang L. High fat diet-triggered non-alcoholic fatty liver disease: A review of proposed mechanisms. Chem Biol Interact. 2020 Oct 1;330:109199. doi: 10.1016/j.cbi.2020.109199. Epub 2020 Aug 15. PMID: 32805210.

Vegas-Suárez, S., Simón, J., Martínez-Chantar, M. L., & Moratalla, R. (2022). Metabolic Diffusion in Neuropathologies: The Relevance of Brain-Liver Axis. *Frontiers in physiology*, *13*, 864263. https://doi.org/10.3389/fphys.2022.864263

Więckowska-Gacek, A., Mietelska-Porowska, A., Chutorański, D., Wydrych, M., Długosz, J., & Wojda, U. (2021). Western Diet Induces Impairment of Liver-Brain Axis Accelerating Neuroinflammation and Amyloid Pathology in Alzheimer's Disease. *Frontiers in aging neuroscience*, *13*, 654509. https://doi.org/10.3389/fnagi.2021.654509