The Effect of Transgenerational Epilepsy on Dementia Pathology in *C. elegans*

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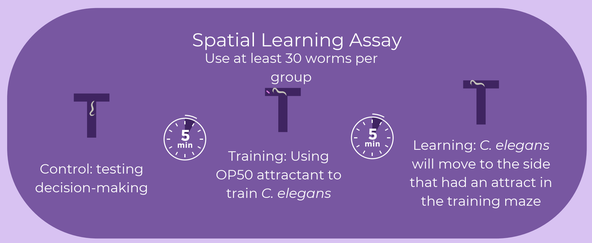
Highlights

- PTZ exposure **impairs spatial learning** in a **dose- and generation-dependent** manner.
- **Cumulative exposure** across generations worsens **learning deficits** in newer generations (G3).
- Some effects of PTZ appear to **persist** even after exposure is stopped, indicating potential **lasting or inherited consequences.**
- Single exposures produce mild effects; repeated exposures produce stronger and more lasting deficits.
- Controls consistently show robust spatial learning.

Background

- **Dementia** – cognitive decline characterized by amyloid beta
- **Epilepsy** – over, uncontrolled activation of neurons
- Have a **bidirectional comorbidity** (Stewart & Johnson, 2025).
- **Epigenetic changes** which can be **inherited** (Fitz-James & Cavalli, 2022).
- Excess **methylation** has been seen in **dementia risk** (Sharma et al., 2020)
- **Seizures** cause **inflammation** (Komada & Nishimura, 2022)
- **C. elegans** is a common **model** organism for **neurological research** (Gorgou et al., 2021)
- **UNC-49** strain is susceptible to seizures when exposed to pentylenetetrazole (PTZ) (Wong et al., 2018)

Methodology



Repeat synchronization and PTZ exposure as needed: 1st gen – none, 2nd gen – once, experimental – twice.

All figures above created by Parnitha Karapakula

Research Question

How does dementia pathology in *C. elegans* change due epilepsy over many generations?

Hypothesis

If more generations of *C. elegans* are given seizures, then the future generations will have more dementia pathology because of inherited epigenetic modifications

Results

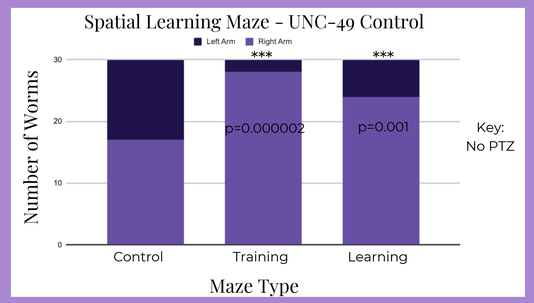


Figure 1. Spatial learning performance of UNC-49 control worms. Maze type, number of worms, and experimental conditions (control, training, and testing) are shown. Statistical comparisons were performed using a Z-test with a population proportion of 0.5 (p = 0.000002, p = 0.001)

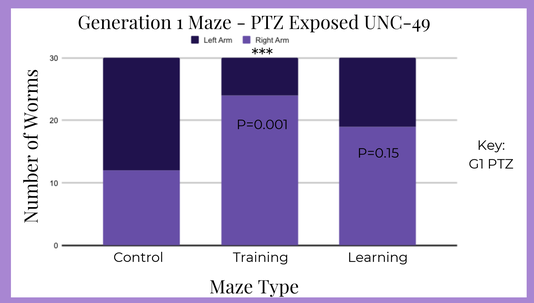


Figure 2. Spatial learning performance of Generation 1 PTZ-exposed UNC-49 worms. Maze type, number of worms, and experimental conditions (control, training, and testing) are indicated. Statistical comparisons were performed using a Z-test with a population proportion of 0.5 (p = 0.001, p = 0.15)

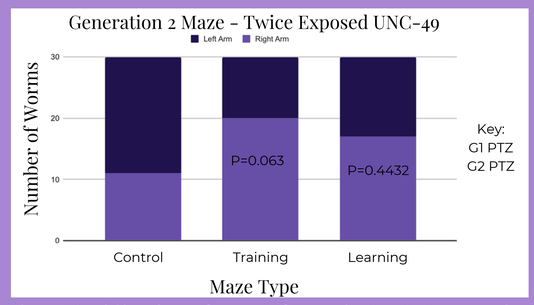


Figure 3. Spatial learning performance of Generation 2 UNC-49 worms twice exposed to PTZ. Maze type, number of worms, and experimental conditions (control, training, and testing) are shown. Statistical comparisons were performed using a Z-test with a population proportion of 0.5 (p = 0.063, p = 0.4432)

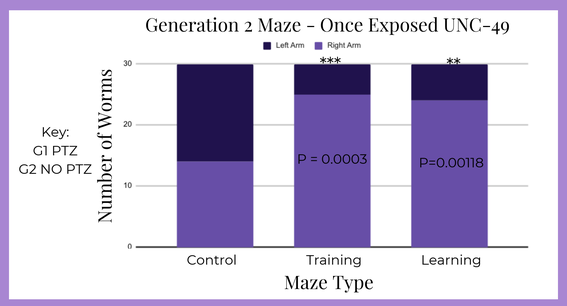


Figure 5. Spatial learning performance of Generation 2 UNC-49 worms once exposed to PTZ. Maze type, number of worms, and experimental conditions (control, training, and testing) are indicated. Statistical comparisons were performed using a Z-test with a population proportion of 0.5 (p = 0.0003, p = 0.00118)

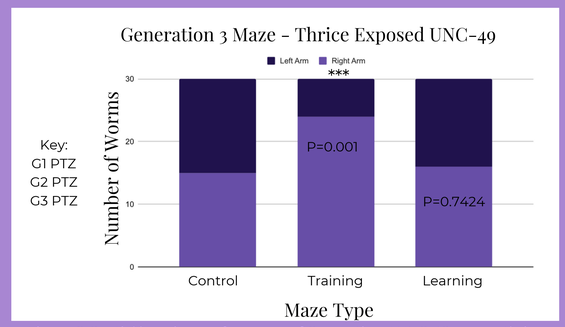


Figure 6. Spatial learning performance of Generation 3 UNC-49 worms thrice exposed to PTZ. Maze type, number of worms, and experimental conditions (control, training, and testing) are shown. Statistical comparisons were performed using a Z-test with a population proportion of 0.5 (p = 0.001, p = 0.7424)

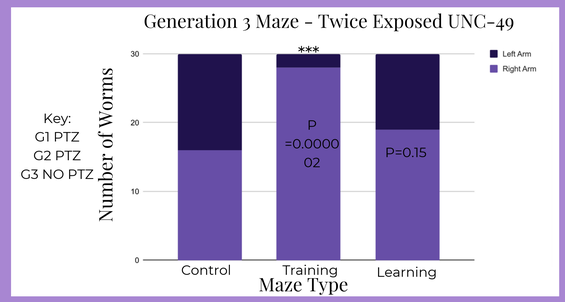


Figure 7. Spatial learning performance of Generation 3 UNC-49 worms twice exposed to PTZ. Maze type, number of worms, and experimental conditions (control, training, and testing) are indicated. Statistical comparisons were performed using a Z-test with a population proportion of 0.5 (p = 0.000002, p = 0.15)

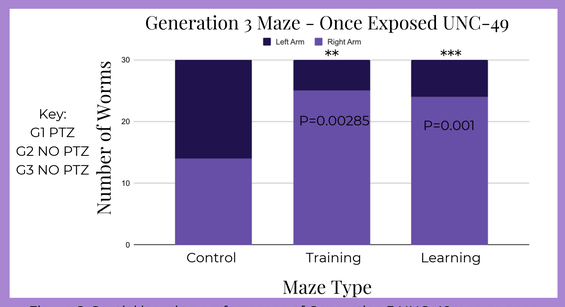


Figure 8. Spatial learning performance of Generation 3 UNC-49 worms once exposed to PTZ. Maze type, number of worms, and experimental conditions (control, training, and testing) are indicated. Statistical comparisons were performed using a Z-test with a population proportion of 0.5 (p = 0.00285, p = 0.001)

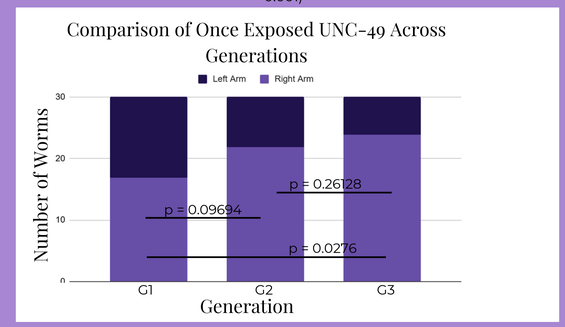


Figure 4. Comparison of spatial learning in once-exposed UNC-49 worms across generations. Number of worms and generation (G1, G2, G3) are indicated. Statistical comparisons were performed using two-proportion Z-tests: G1 vs G2 (p = 0.09694), G2 vs G3 (p = 0.26128), and G1 vs G3 (p = 0.0276)

Future Steps

- Quantify **amyloid-beta accumulation** in the brains of each generation using Thioflavin-T staining.
- Measure **methylation levels** across generations.
- Analyze the relationship between **seizure severity, frequenc**y and **spatial learning** performance.
- Evaluate whether **antioxidant treatment** can prevent or reduce the spatial learning deficits observed following seizures.