

The Effect of Transgenerational Epilepsy on Dementia Pathology

Parnitha Karapakula

- PTZ Exposure **worsens spatial learning** in a **dose- and generation-dependent** manner, with cumulative exposure causing stronger deficits
- Some of the effects **persist** after exposure stops, suggesting **lasting or inherited consequences**

Research Question

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

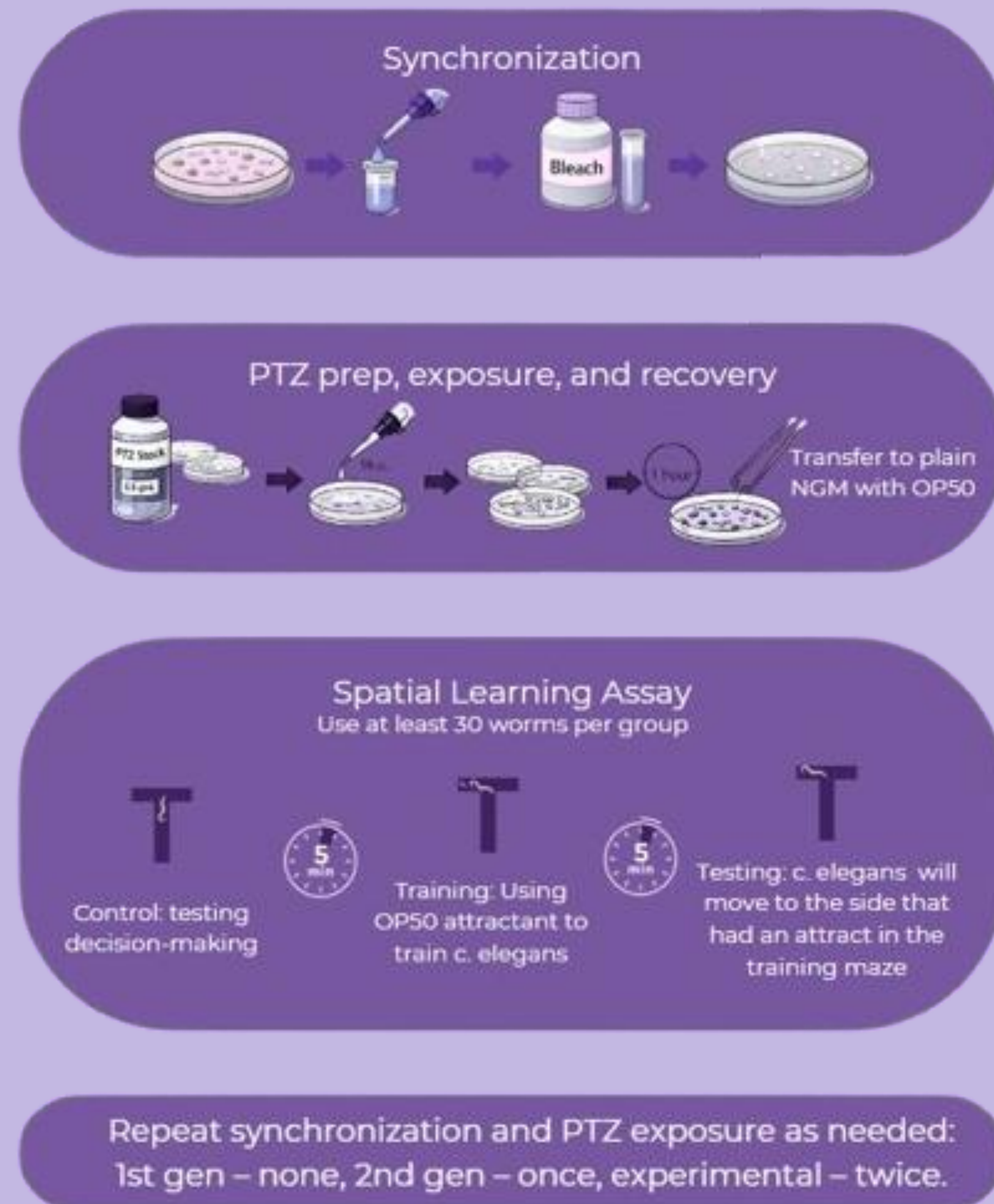
Hypothesis

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

Background

- Dementia** – cognitive decline (amyloid beta); **epilepsy** – uncontrolled neurons; **bidirectional comorbidity** (Steward & Johnson, 2025)
- Epigenetic changes** – heritable (Fitz-James & Cavalli, 2022)
- Excess methylation** – increases **dementia risk** (Sharma et al., 2020)
- Seizures** → **inflammation** (Komada & Nishimura, 2022)
- C. elegans*** – common **model organism** (Gorgou et al., 2021)
- UNC-49 strain - PTZ-induced seizures** (Wong et al., 2018)

Methodology



Results

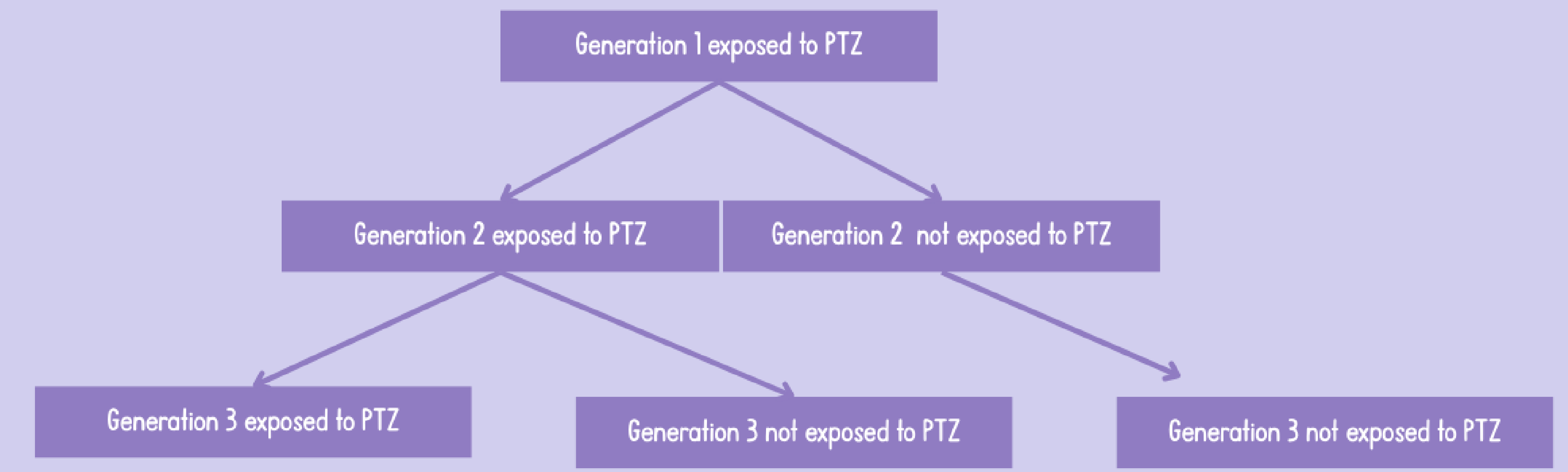


Figure 1. Flow chart of exposure groupings of the generations of UNC-49 worms. Generation 1 worms that were exposed to PTZ, and subsequent generations were divided into exposed and non-exposed groups. This design allowed assessment of both direct and transgenerational effects of PTZ exposure on spatial learning.

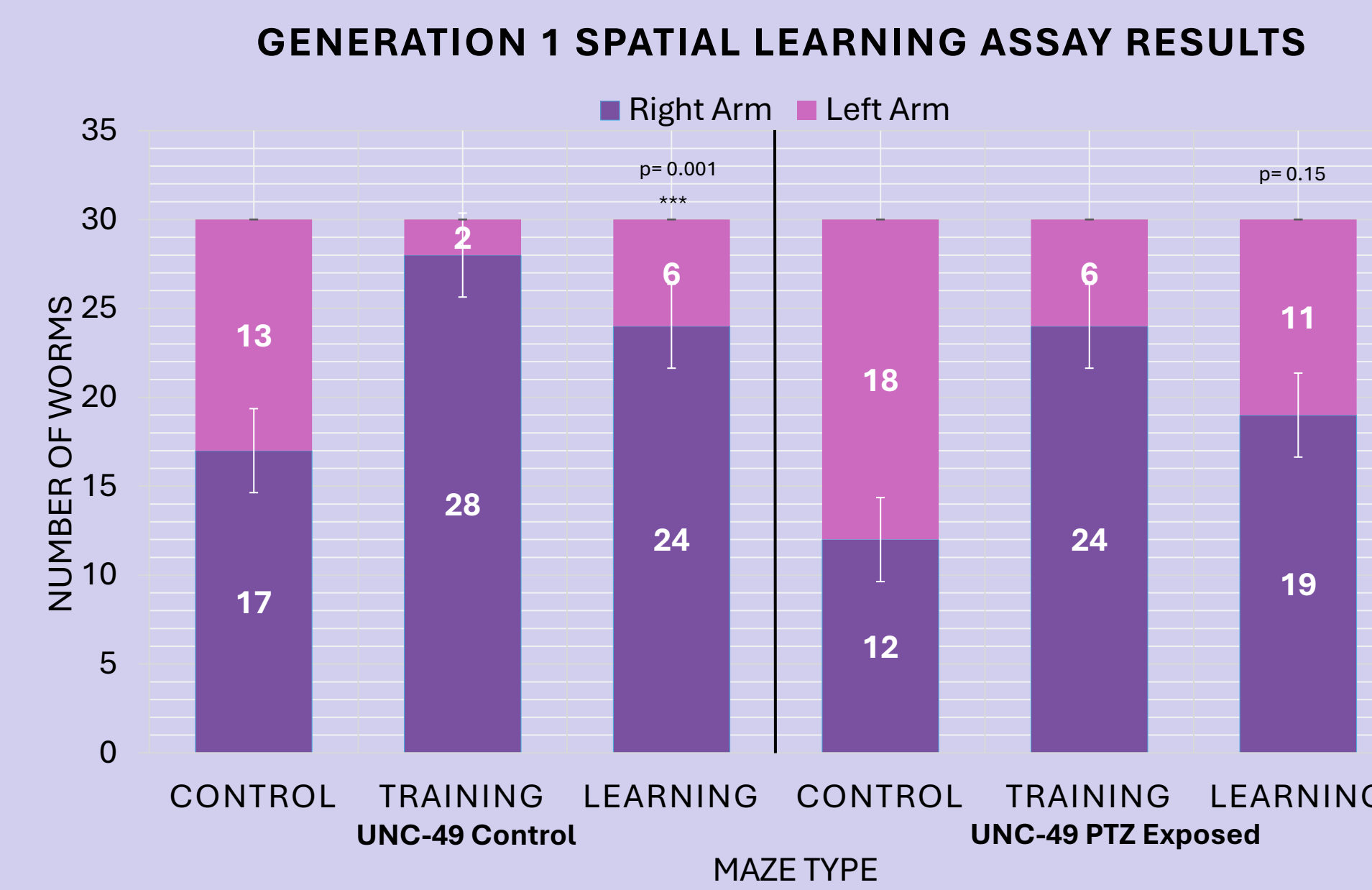


Figure 2. Spatial learning performance of Generation 1 worms with and without PTZ exposure. Control (no PTZ) worms showed a significant learning index ($p=0.001$). PTZ-exposed worms showed a learning deficit with a z test value showing a significance level of $p=0.15$. This suggests that PTZ impaired retention of spatial learning.

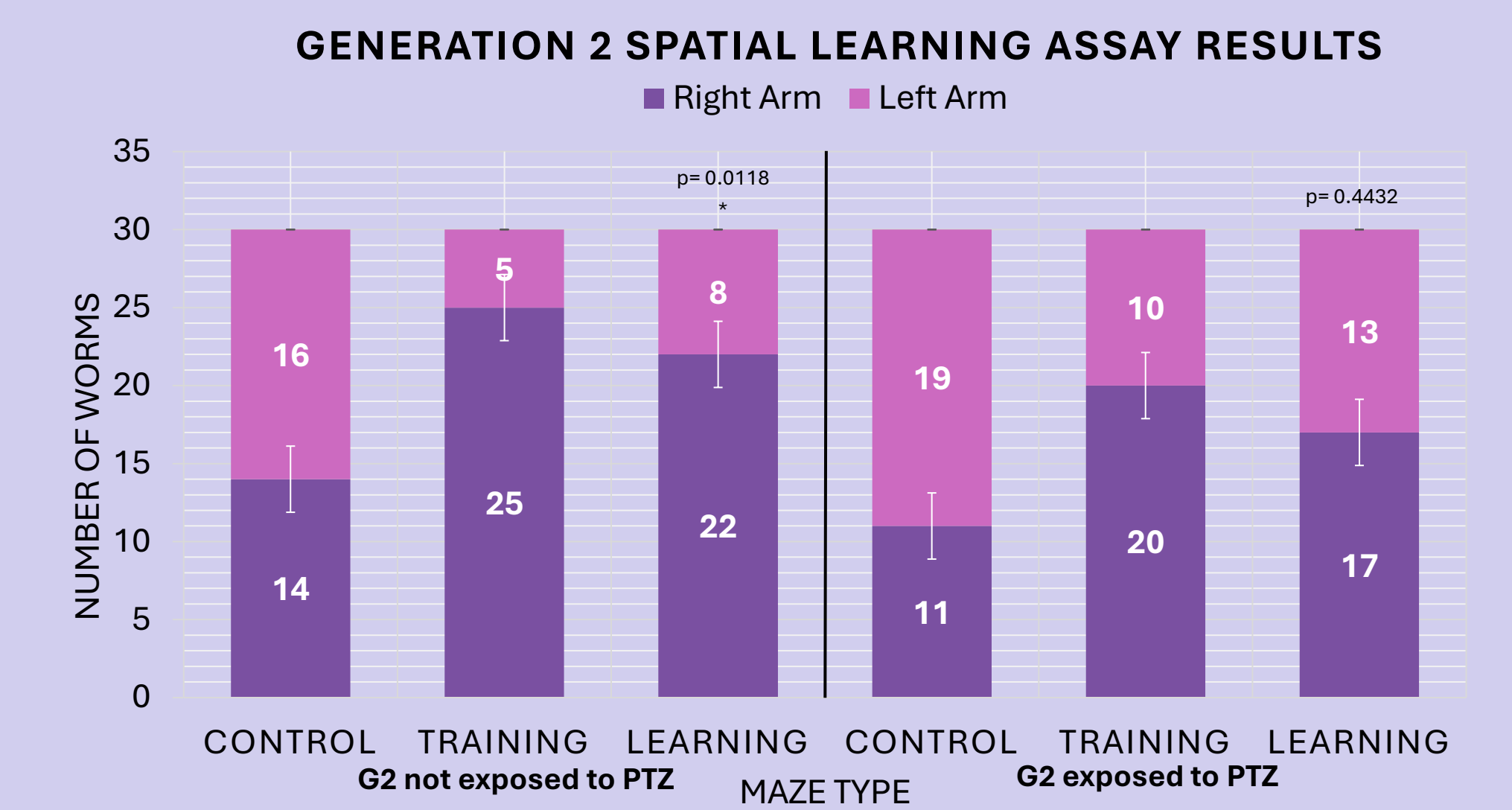


Figure 3. Spatial learning performance of Generation 2 UNC-49 worms following single and double PTZ exposure. After one PTZ exposure, worms showed a significant arm preference during learning ($p=0.018$), indicating improved spatial learning. In contrast, worms exposed twice showed no significant arm preference when compared to chance in a one-proportion z-test. ($p=0.4432$). This suggests impaired learning.

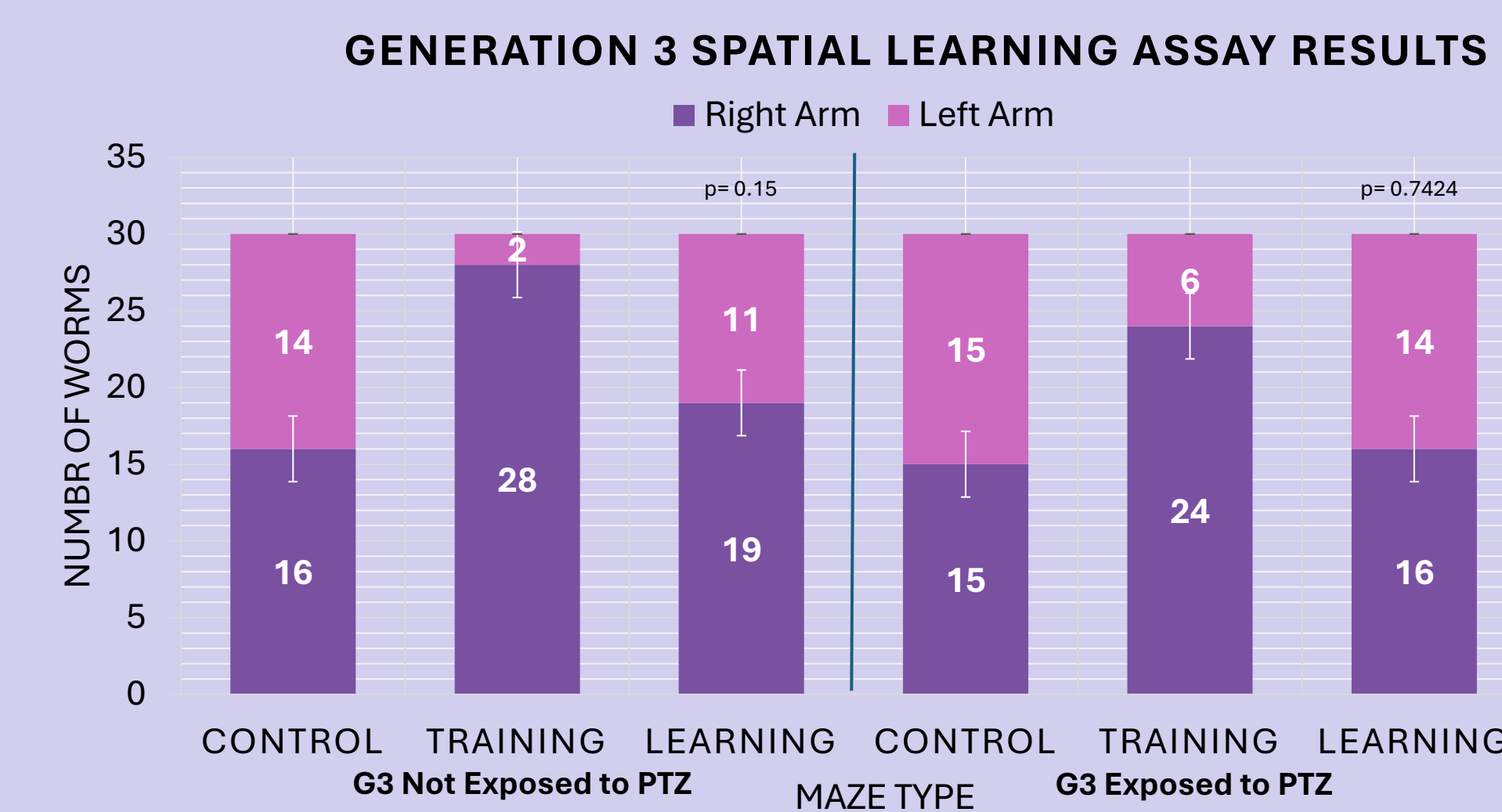


Figure 4. Spatial learning performance of generation 3 UNC-49 worms. During learning, worms exposed twice and thrice showed no significant arm preference ($p=0.15$, $p=0.7424$). These results indicate that impaired spatial learning, as a z-test, shows that there is no significant difference from complete chance.

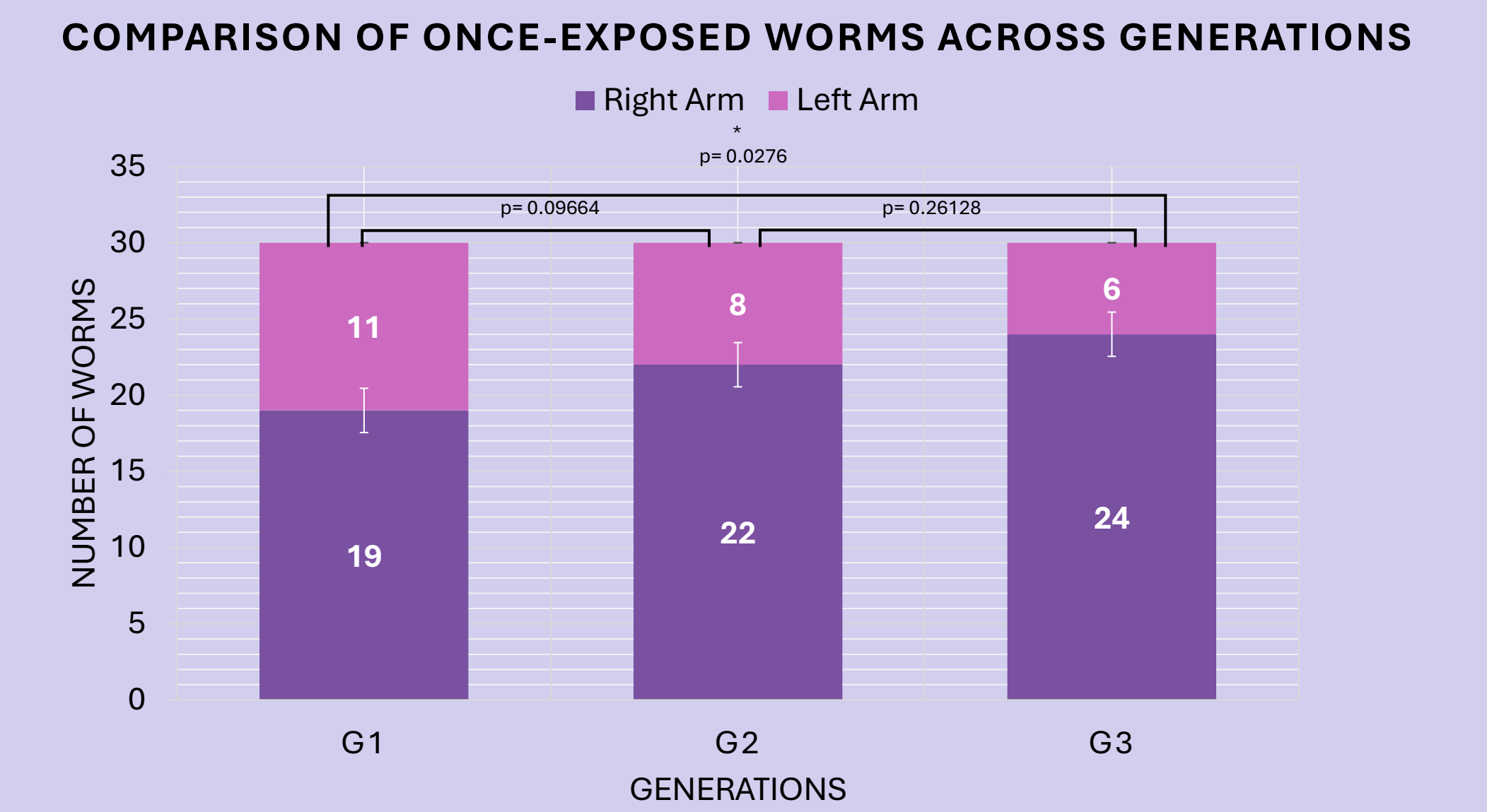


Figure 5. Comparison of spatial learning in once-exposed UNC-49 worms across generations. The number of worms and generation (G1, G2, G3) are indicated. Statistical comparisons were performed using two-proportion Z-tests: G1 vs G2 ($p=0.09664$), G2 vs G3 ($p=0.26128$), and G1 vs G3 ($p=0.0276$).

Future Steps

- Quantify amyloid beta accumulation using thioflavin T staining
- Measure methylation levels across generations
- Test on other seizure-susceptible *C. elegans* strain

- Analyze the relationship between seizure severity, frequency, and spatial learning
- Evaluate if antioxidant treatment can reduce spatial learning deficits