

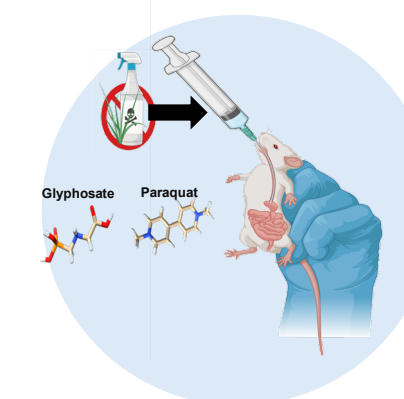
Abstract

Globally used environmental toxins such as paraquat and glyphosate have been linked to oxidative stress and progressive dopaminergic dysfunction which are predominant features of neurodegenerative disorders such as Parkinson's disease (PD). Although Parkinson's disease has been studied for decades, its precise etiology remains unsolved.

In this study, after 30 days of herbicide exposure we used preclinical MRI to characterize the microstructural integrity and water diffusivity in the rodent brain, in parallel we conducted behavioral assays to evaluate motor coordination and spatial memory. This integrated framework provides better insight into characterizing the neurodegenerative effects of toxin exposure.

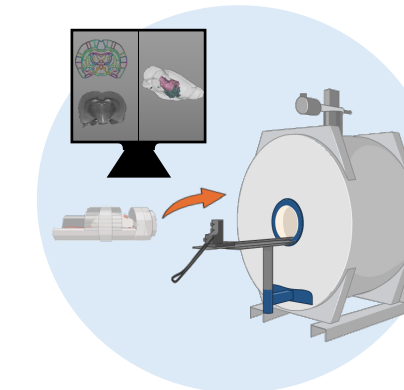
Experimental Design

Adult Sprague-Dawley male ($N=18$) and female ($N=18$) rats staggered into 3 Cohorts vehicle, Paraquat, Glyphosate with each consists of 6 males and 6 females received daily oral dosage from Day 1–45. Diffusion-weighted imaging (DWI) was performed on Day 31. rmTBI was induced on Day 32–34. Behavioral assessment were occurred on Days 35–39. 2 weeks post-injury, fMRI, Functional connectivity and a follow up DWI was performed. finally, tissues were collected for further biomarker evaluation



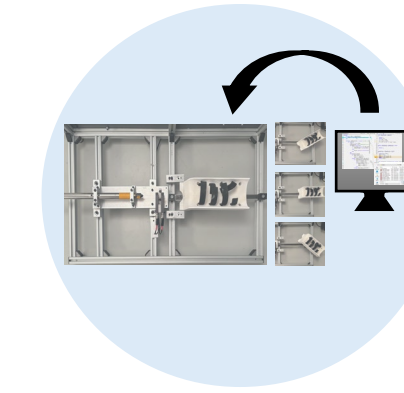
Day 1- 45 Oral gavage treatments

- Vehicle (saline) → administered every 3rd day
- Paraquat (10 mg/kg) → administered every 3rd day
- Glyphosate (75 mg/kg) → administered everyday



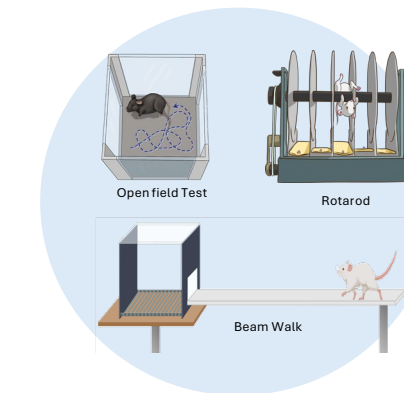
Day 31 Neuroimaging → Pre-injury

- 7.0 T Magnetic Resonance Imaging
- T2 weighted anatomy
- Diffusion Weighted Imaging (DWI)



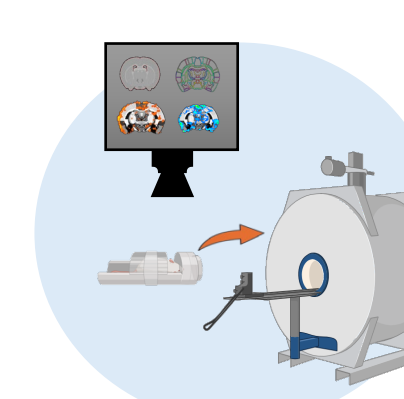
Day 32-34 Repetitive mild traumatic brain injury (rmTBI)

- Buprenorphine (subcutaneous) – Extended release (ER) 0.1 mg/kg
- Performed rmTBI using a controlled impactor (7.4 m/s) over 3 consecutive days.



Days 35-39 Behavioral Assays

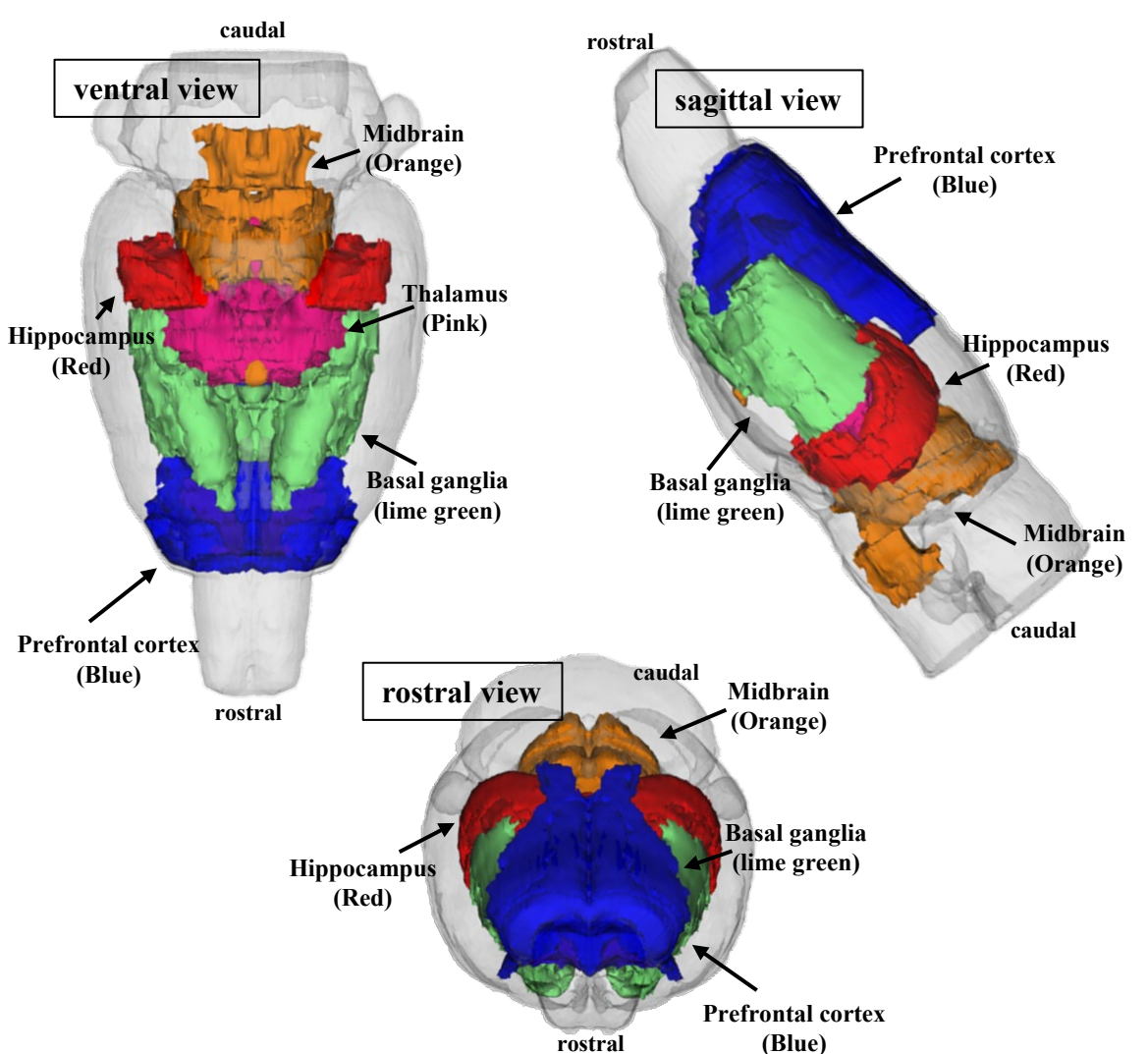
- Open Field Test (OFT)
- Novel Object Recognition (NOR)
- rotarod
- beam walk.



Day 45 Neuroimaging Post- Injury

- 7.0 T MRI , T2-weighted anatomy
- Functional connectivity , fMRI (hypercapnic, benzaldehyde induced reward stimulus challenge)
- Diffusion Weighted Imaging (DWI)
- Post- Tissue collection → biomarker evaluation

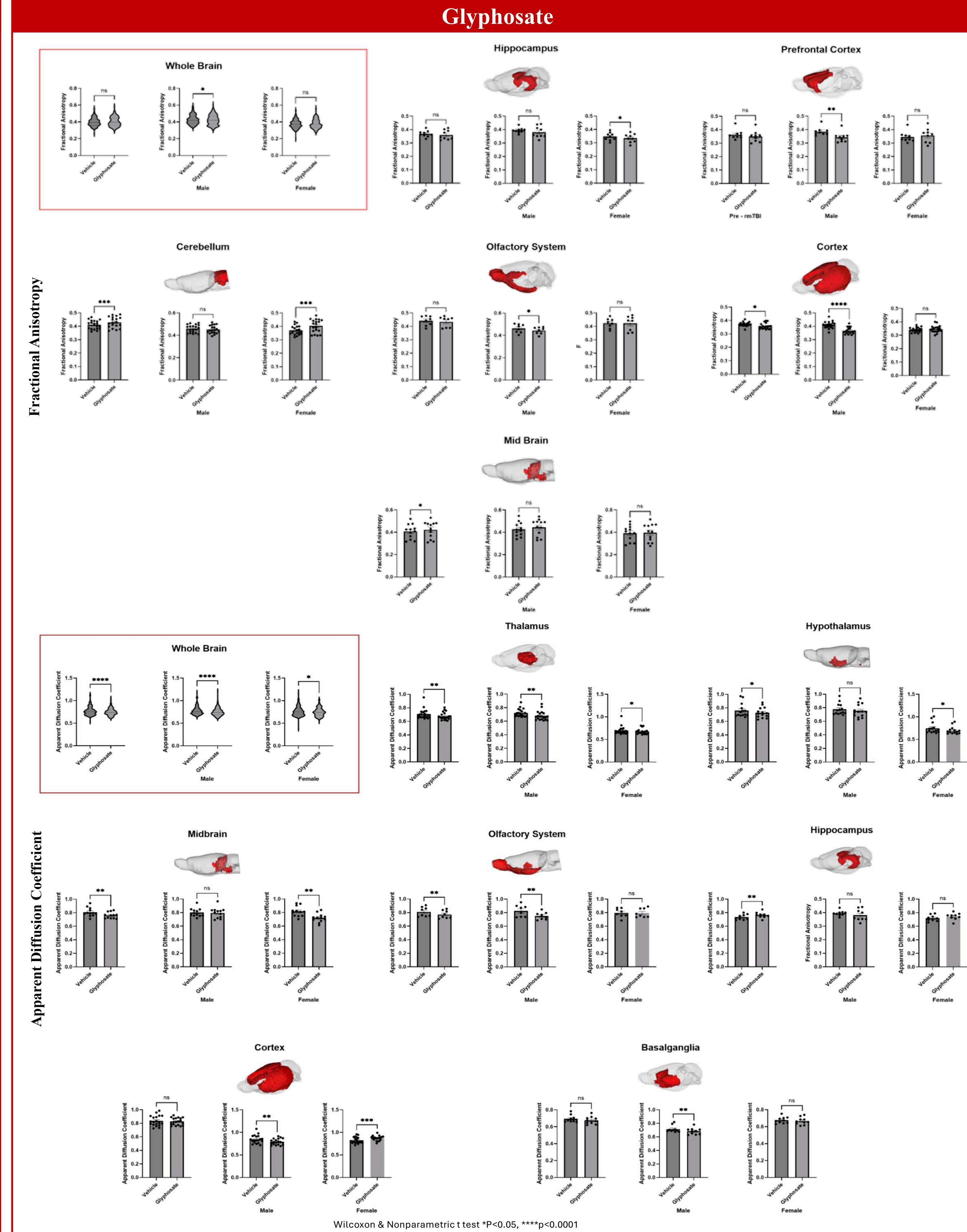
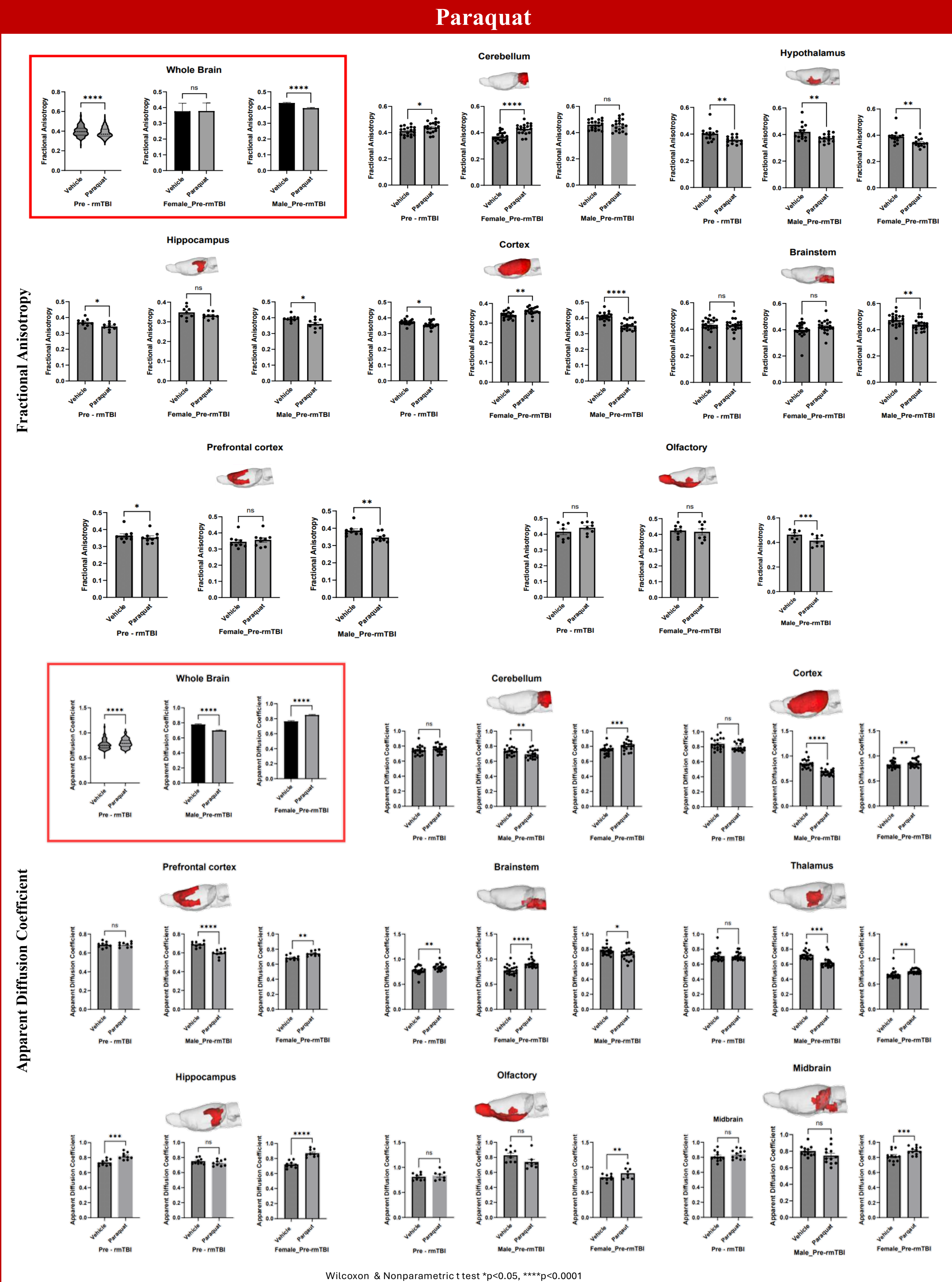
3D reconstruction of affected Brain regions



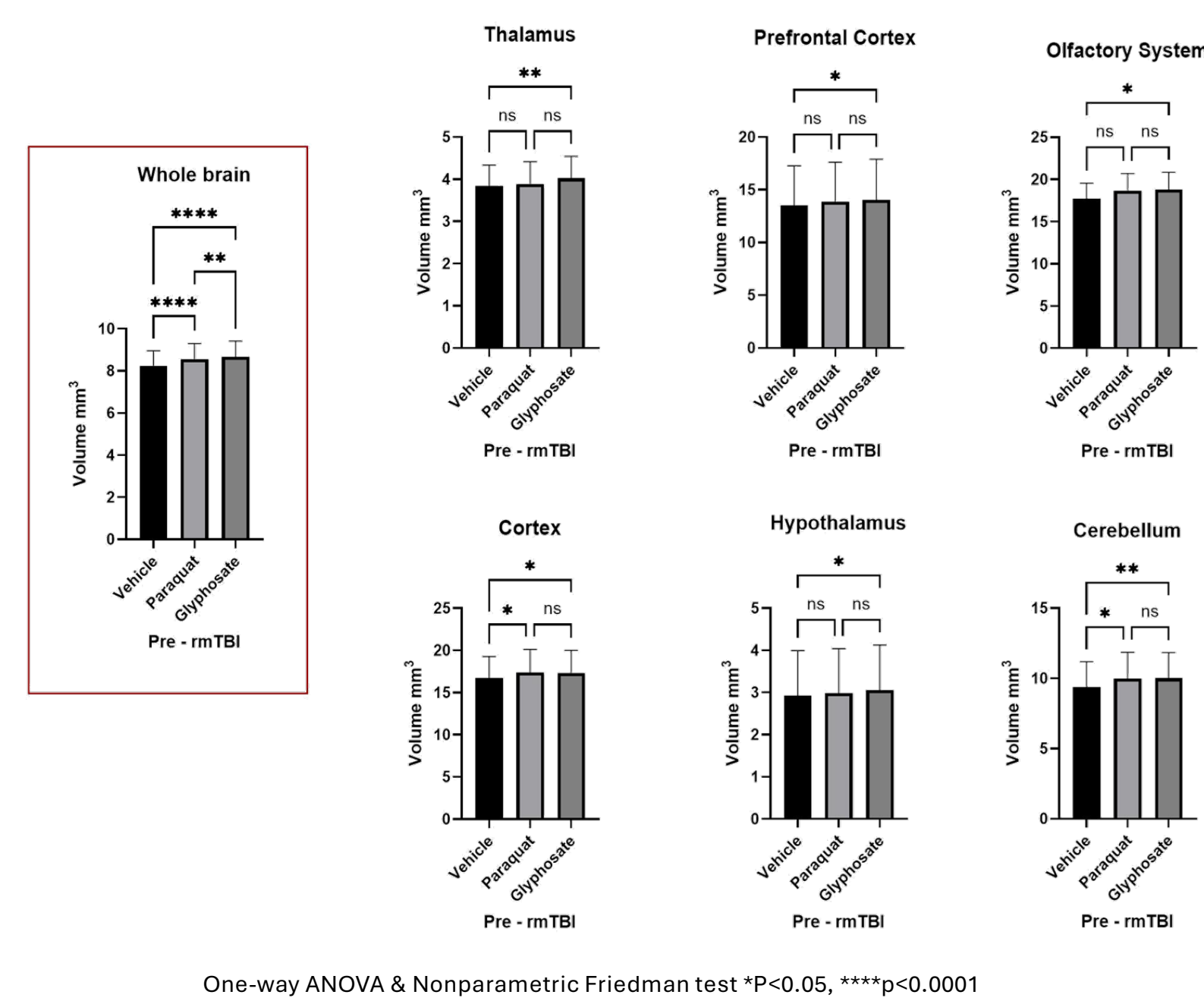
DWI results exhibited a significant alterations

Following 30 days of herbicide exposure, diffusion weighted imaging showed microstructural changes in dopaminergic-rich regions, including midbrain, basal ganglia, thalamus, prefrontal cortex, and hippocampus. These changes were characterized by restricted water diffusion, suggesting early structural disruption in brain regions. Potentially affect nigrostriatal pathway the major dopaminergic circuit pathway which is affected in Parkinson disease

Diffusion Weighted Imaging (DWI) Results



Volumetric Based Morphometry Day - 30



Discussion

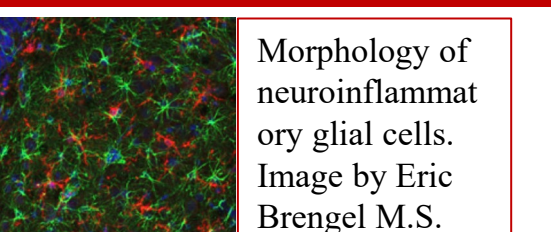
- Changes in FA and ADC following paraquat and glyphosate exposure suggest early microstructural changes in brain regions which are highly vulnerable in Parkinsonian neurodegeneration.
- In males, widespread reductions in FA and ADC across the brain regions likely reflect microstructural changes, consistent with mechanisms that increased in cellular density (cytotoxic edema) and loss of white matter integrity.
- In contrast, females often showed increased ADC or FA across the regions which may indicate vasogenic edema, or loss of axonal fibers.
- Notable, region-specific changes in dopaminergic regions and increased brain's volume after herbicide exposure reflects the neuroinflammation and possible oxidative stress.

Future Direction

Immunohistochemistry will be conducted to identify dopaminergic markers such as α -synuclein and tyrosine hydroxylase as well as microglial activation. Biomarker evaluations will assess metabolic dysfunction and systemic inflammation, enabling mechanistic insight into herbicide induced neuroinflammation and oxidative stress

Acknowledgement

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- Ekam Center for our MRI imaging technology
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Morphology of neuroinflammatory glial cells. Image by Eric Brengel M.S.

