MRI micro- and macro-structural biomarkers linked to nonpathological brain aging in macaques

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Introduction

Using a robust Magnetic Resonance Imaging (MRI) microscopy battery composed of

- Diffusion MRI (dMRI)
- Relaxometry based MRI (rMRI)

Goal: To quantify changes in brain structure related to normal aging.

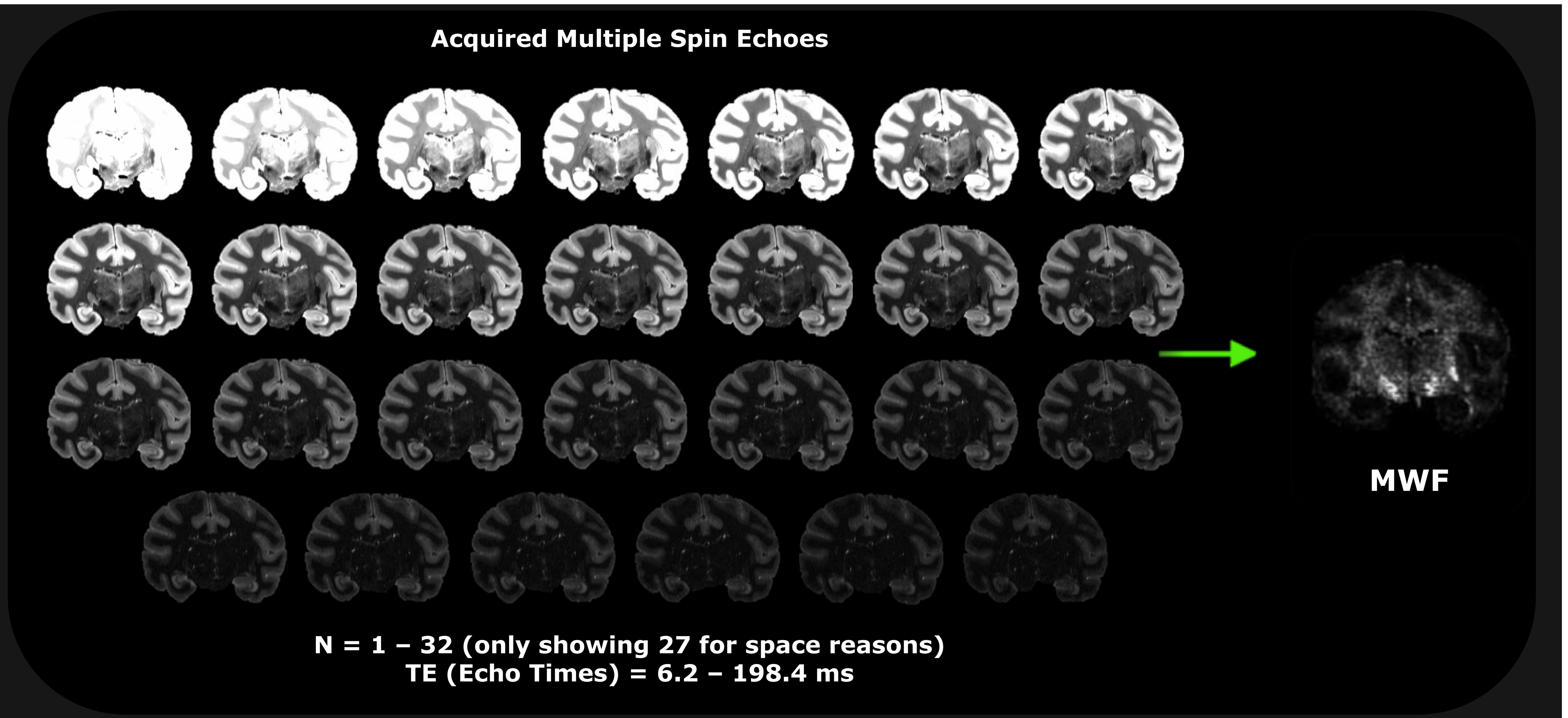
- Cohort Size**:** 12 female non-human primates (bonnet macaques) brains provided by the Barnes lab.
- Ages ranging from 10 to 25 years old (30 to 75 human equivalent years).

Ex-vivo MRI battery is developed to examine brain specimens at high resolution (***200-600 micron scale***) for quantitative biomarkers that indicate age-related brain dysfunction.

Background

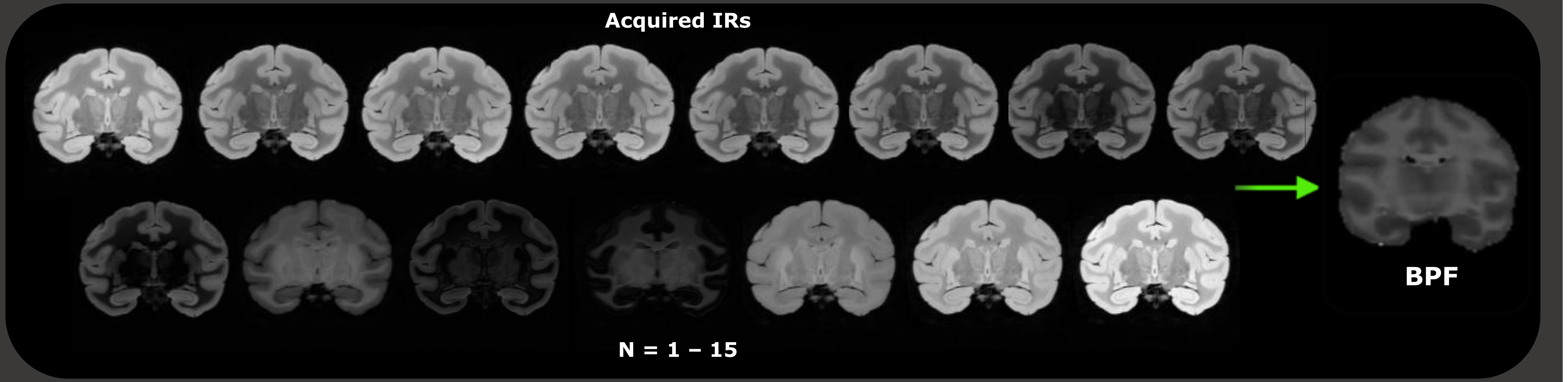
Multiple Spin Echo (MSE) – rMRI Technique:

Myelin Water Fraction (MWF) – Quantifies water trapped between myelin bilayers (a marker for myelin content – quantifies myelin found in each voxel).



Selective Inversion Recovery (SIR) – rMRI Technique:

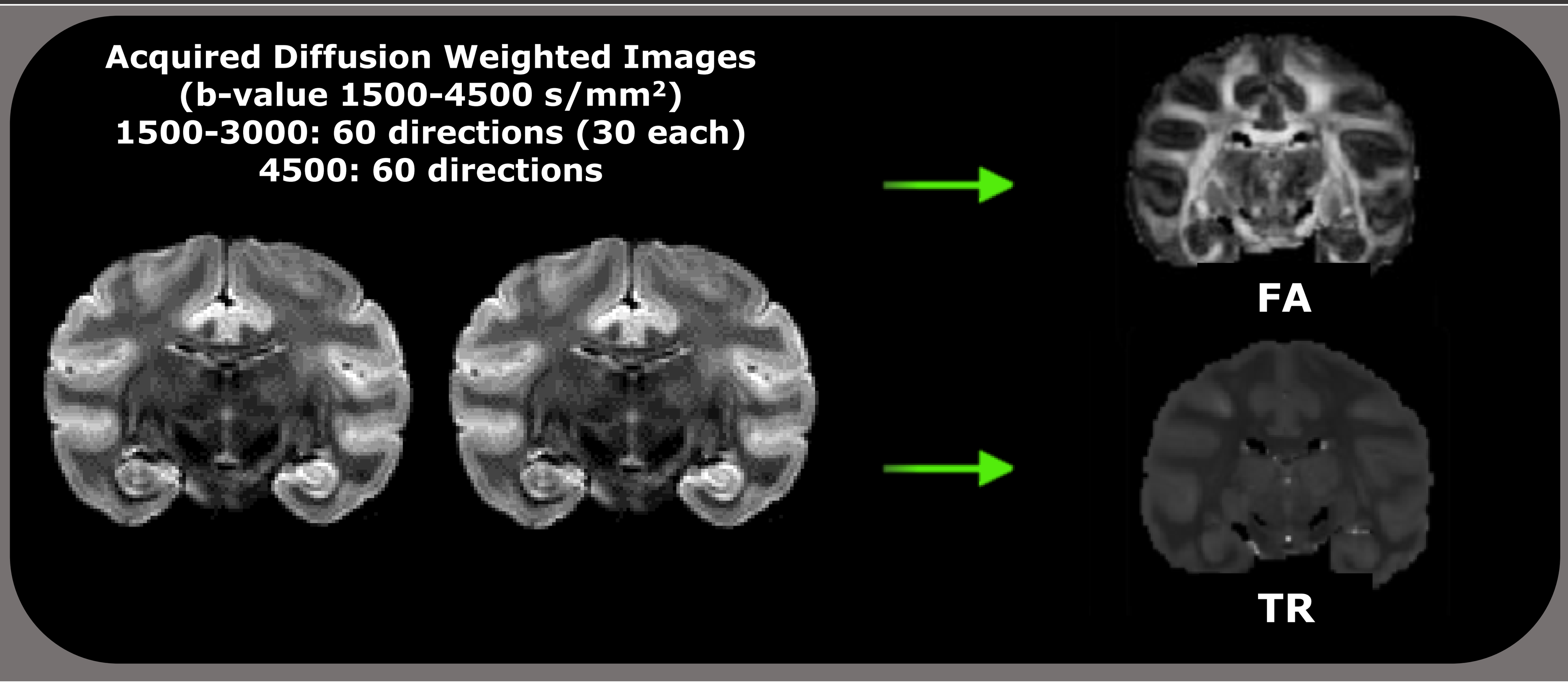
Bound Pool Fraction (BPF) – Measures myelin content and is sensitive to molecular size.



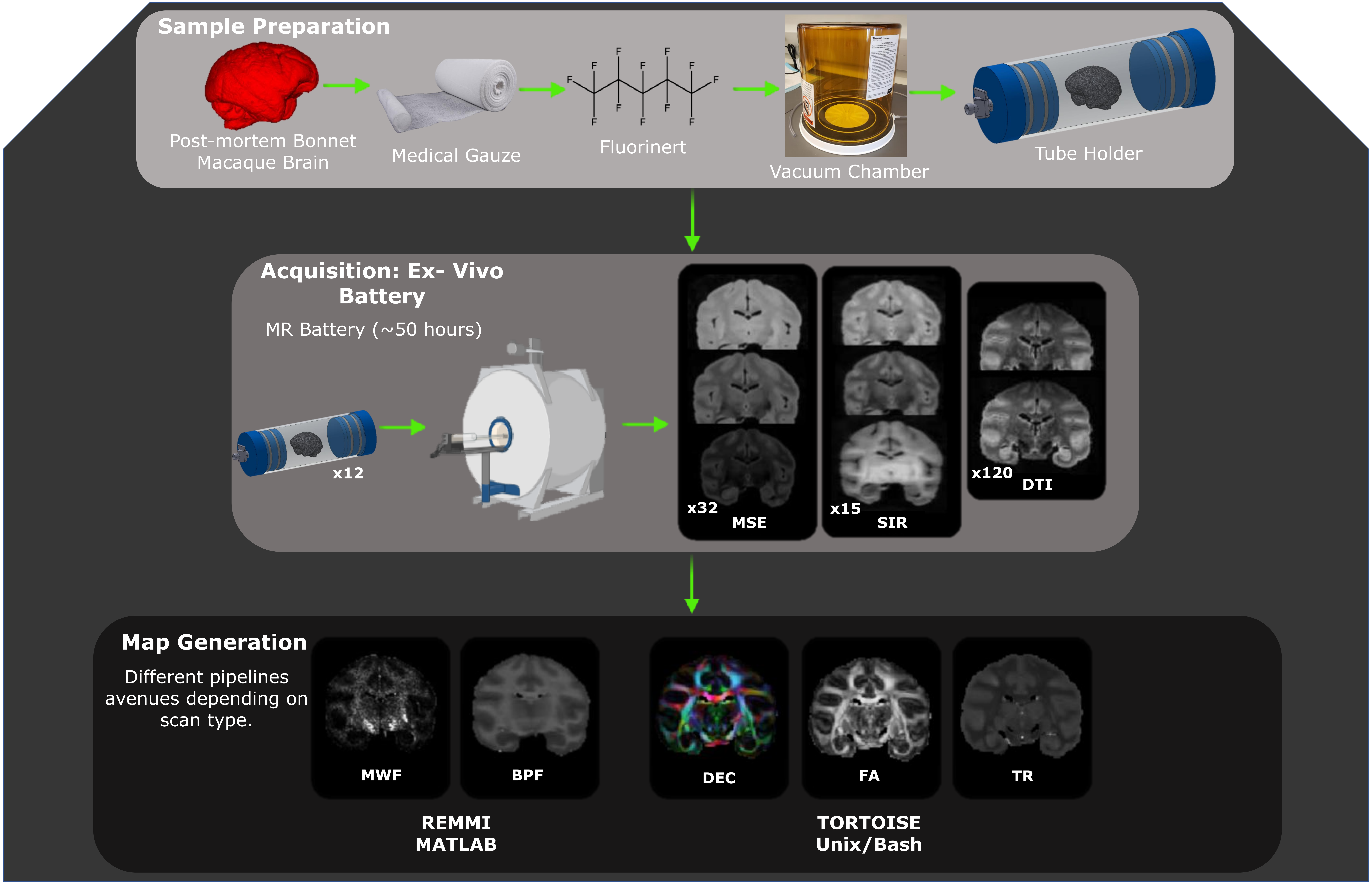
Diffusion Tensor Imaging (dMRI):

Fractional Anisotropy (FA) – Reports that there is a preferred direction of water diffusion in each voxel.

Trace (TR) – Reports the total water diffusion regardless of direction.



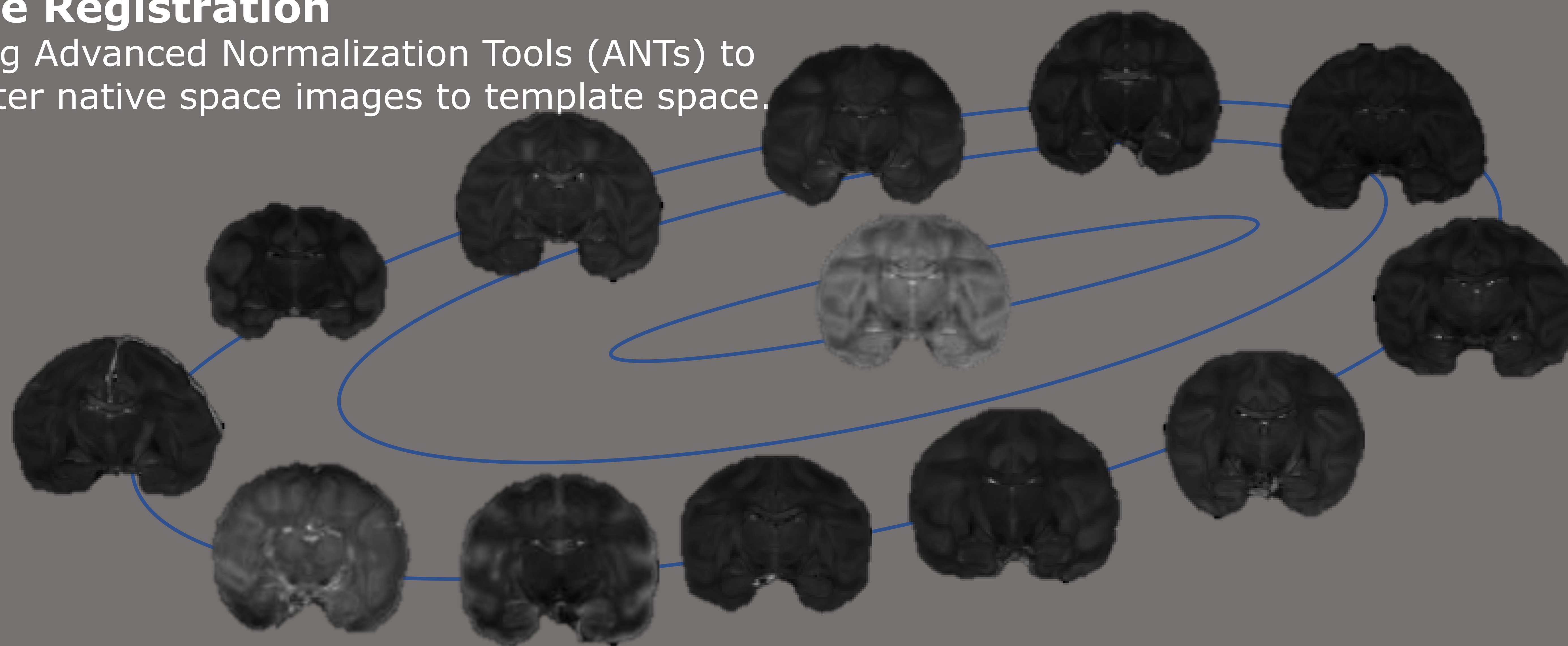
Summary of Methods



Summary of Methods

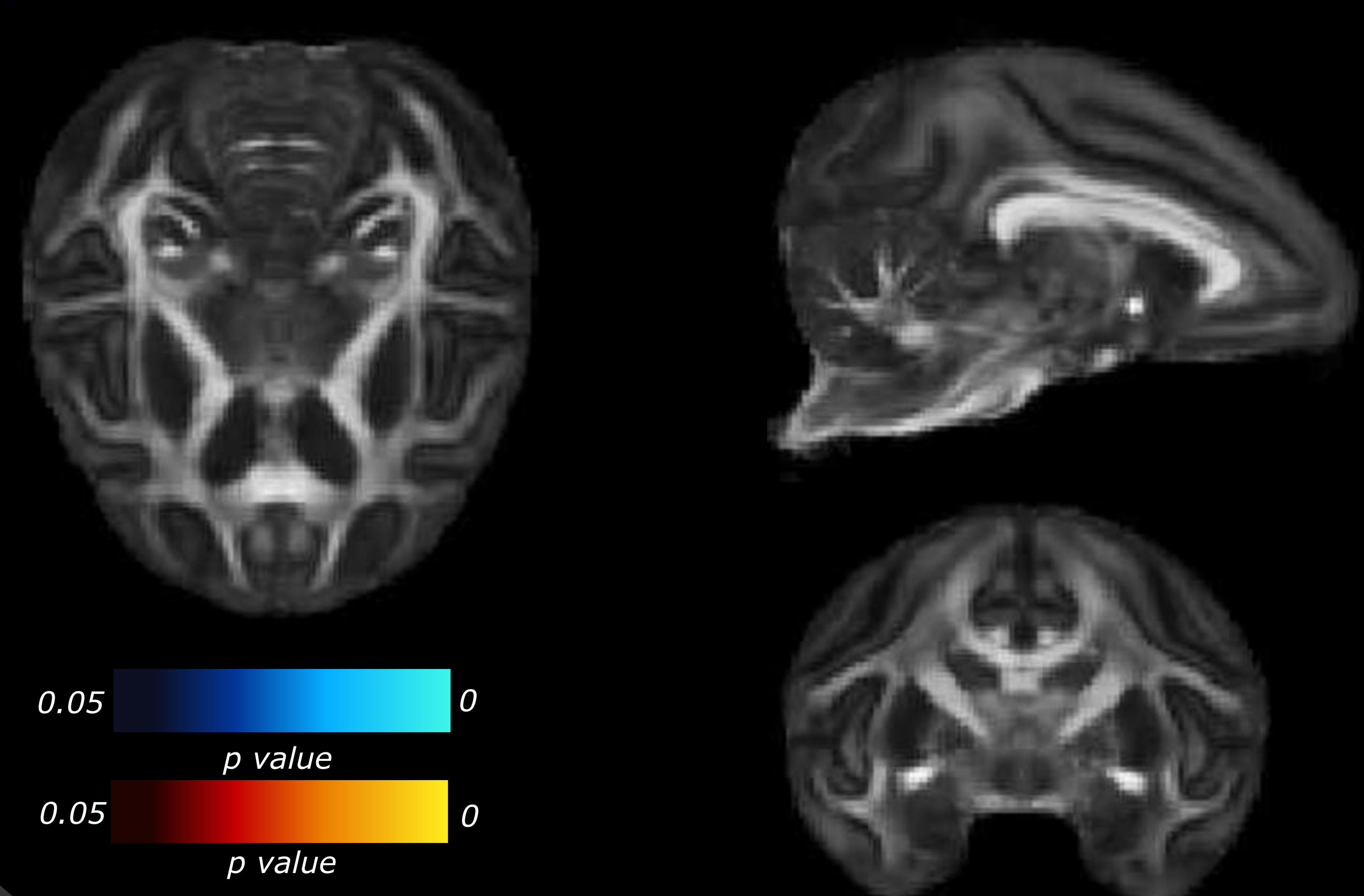
Image Registration

Using Advanced Normalization Tools (ANTs) to register native space images to template space.



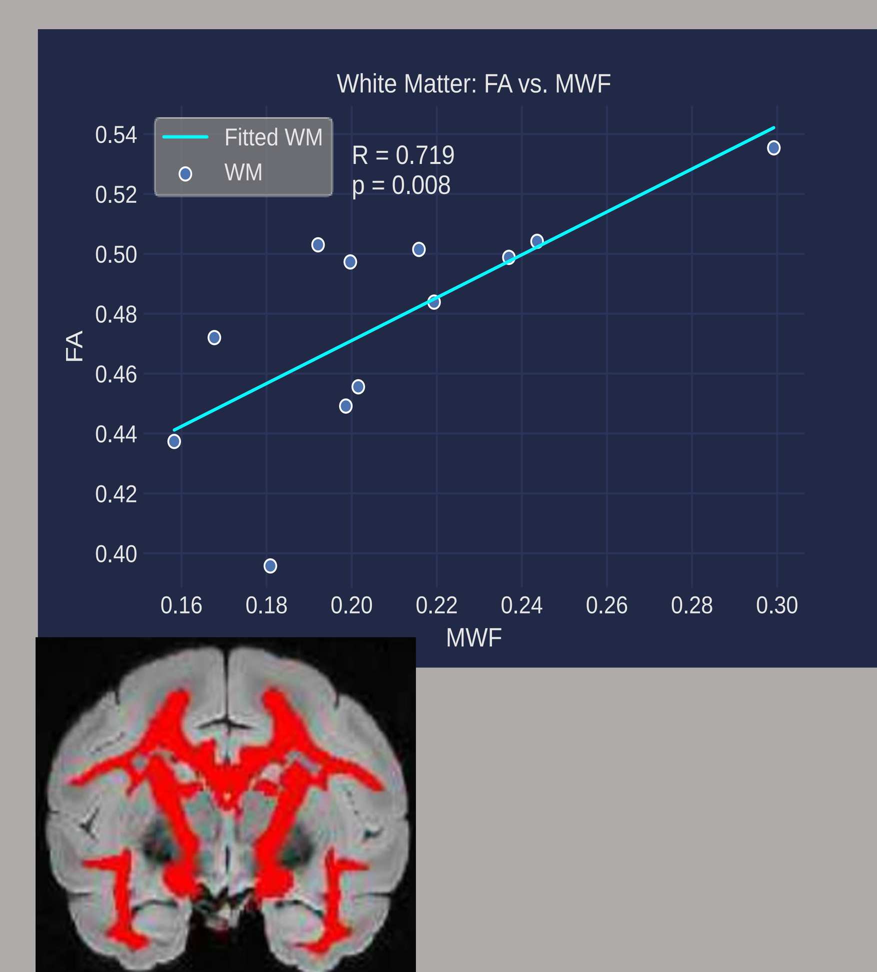
Voxel-wise Analysis

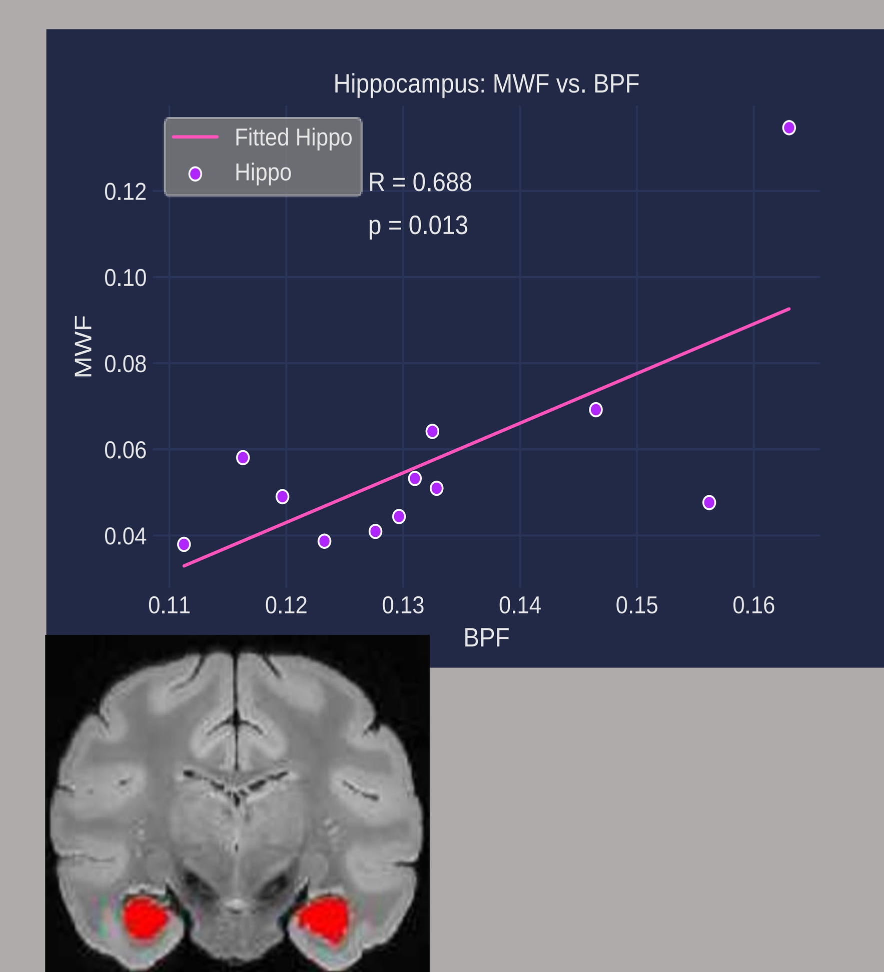
Using fsl randomise tool threshold free cluster enhancement and assessing negative and positive correlations with age.



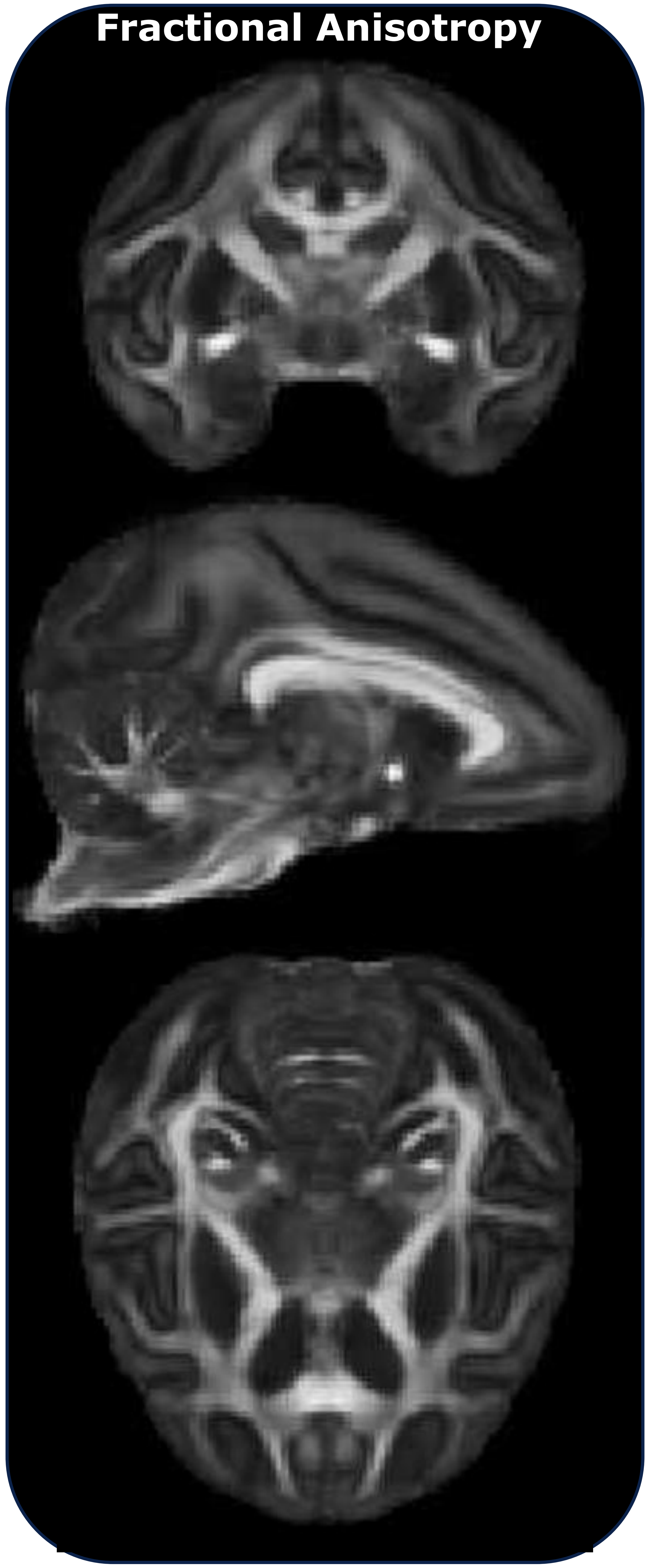
ROI Analysis

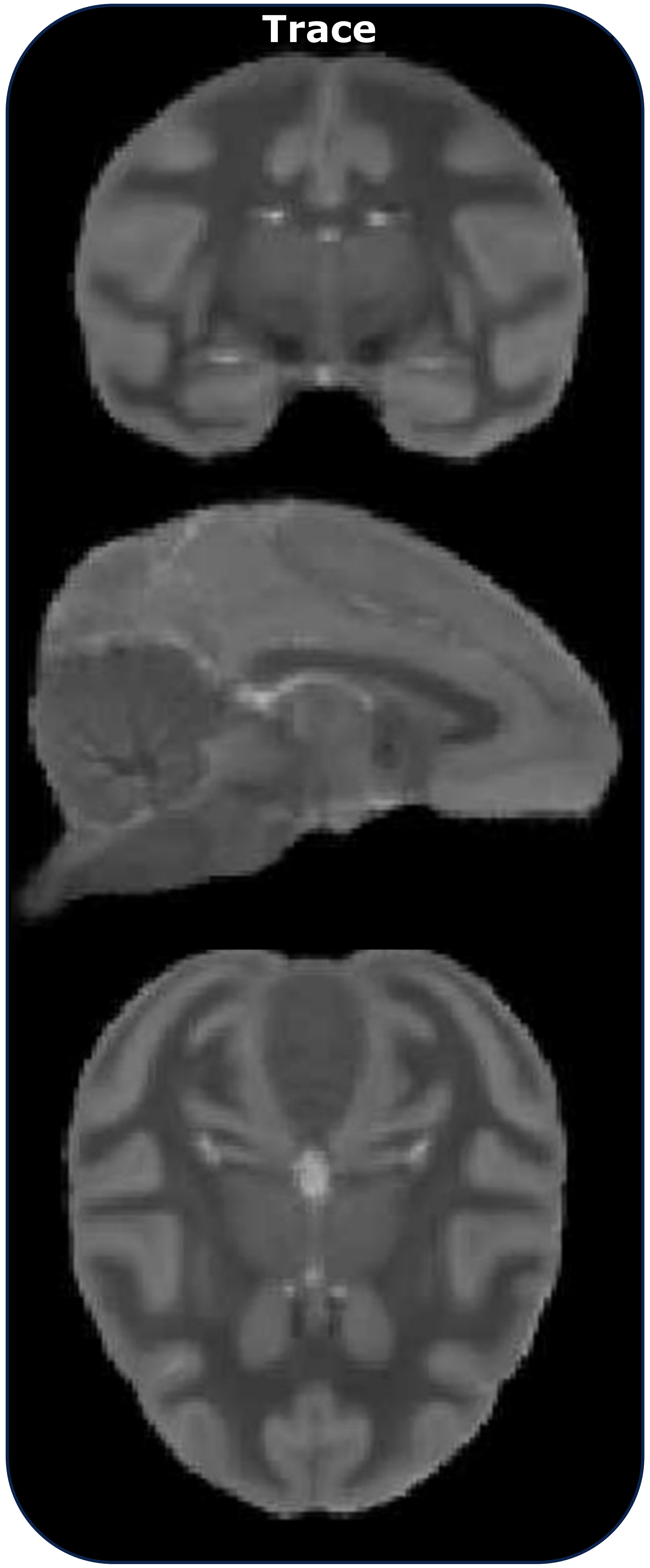
Masked high resolution anatomical (HRA) and conducted a Pearson correlation test across cohort.

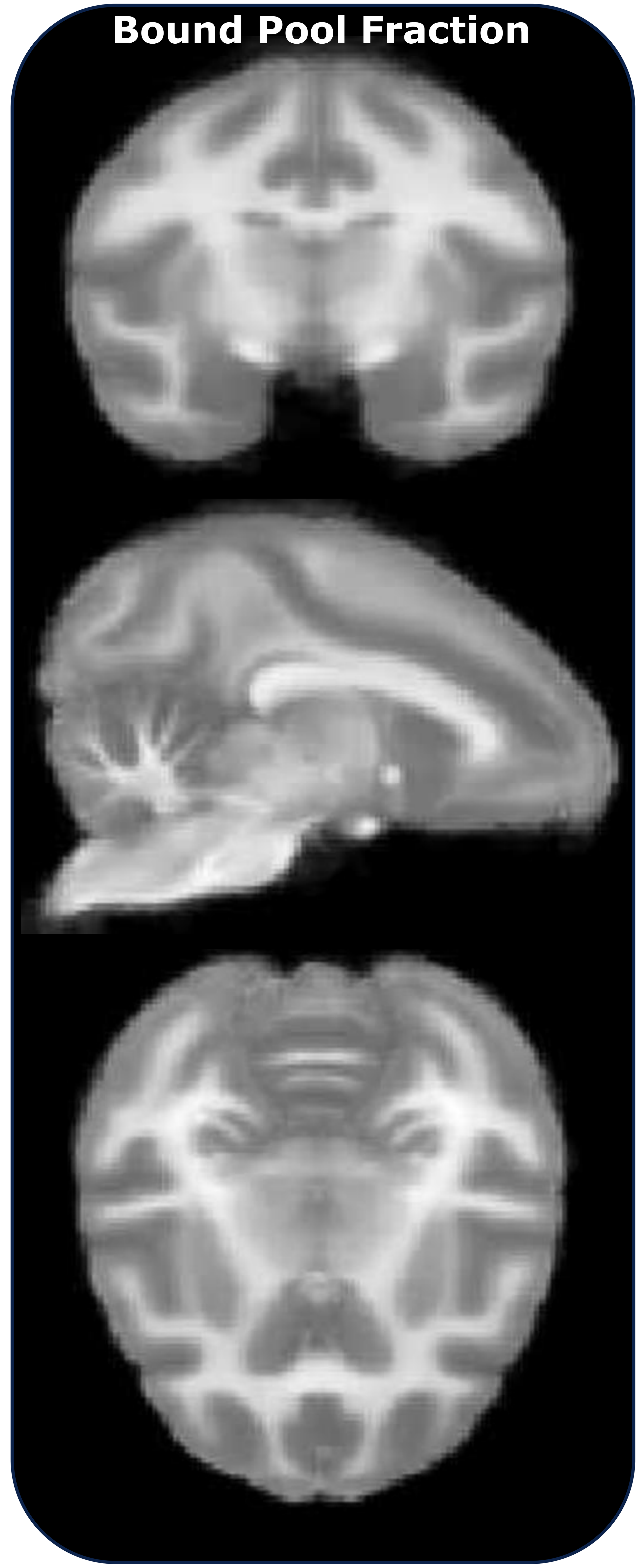


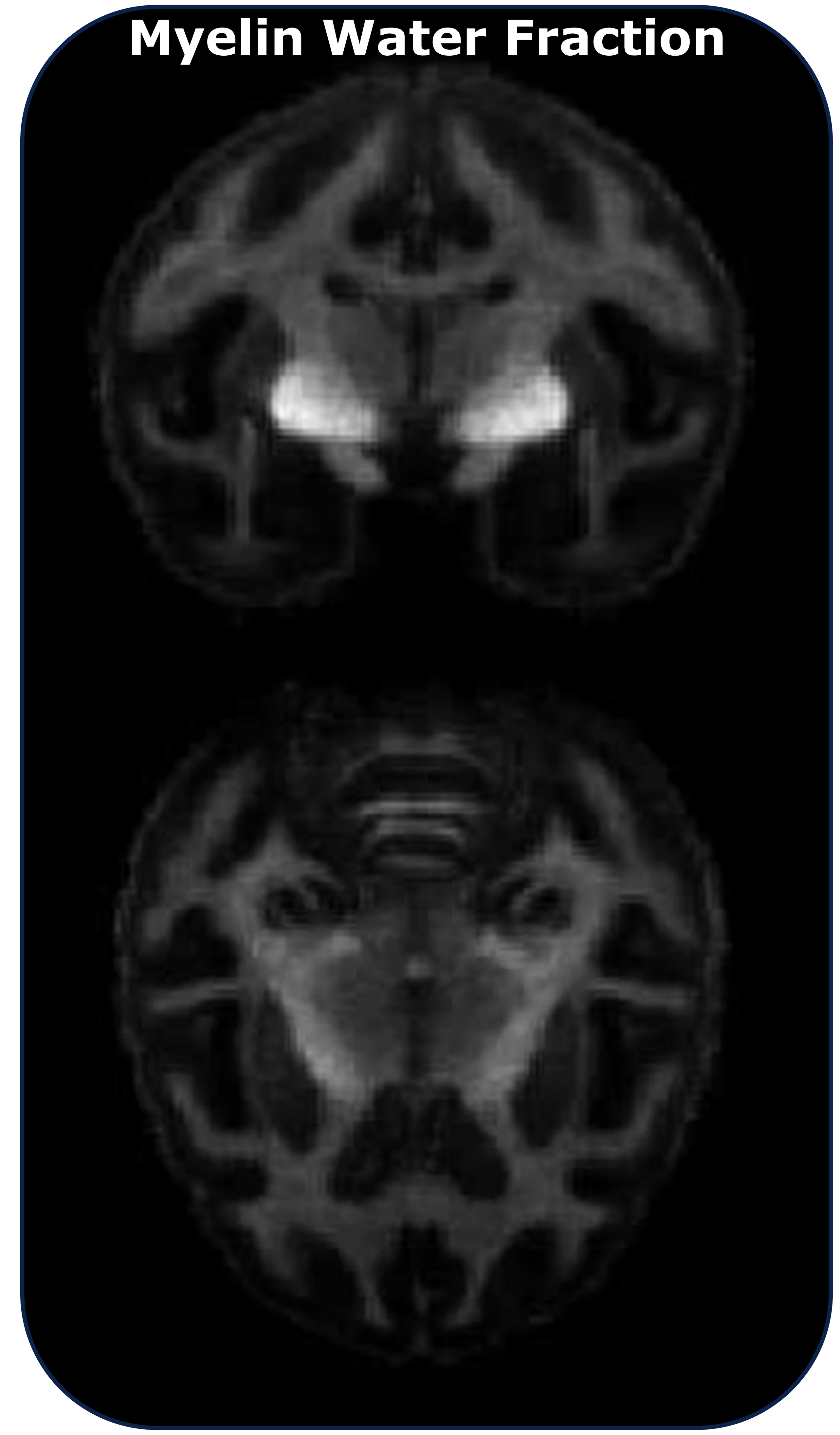


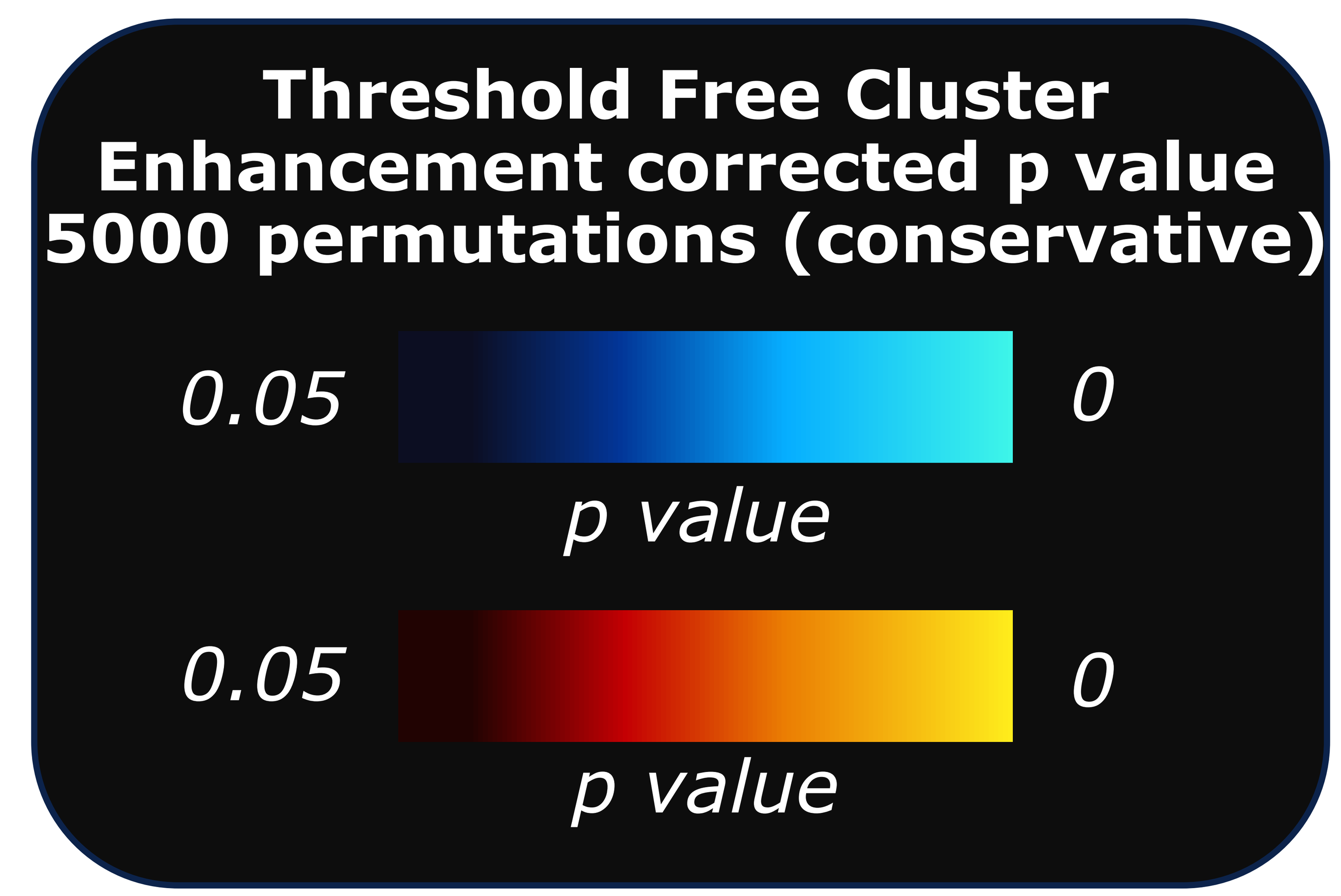
Results – Voxel-wise Analysis











Results – ROI Analysis

- Found strong correlations when assessing interactions between different MR metrics to one another.

Conclusions

In Voxel-wise and ROI analysis with respect to aging:

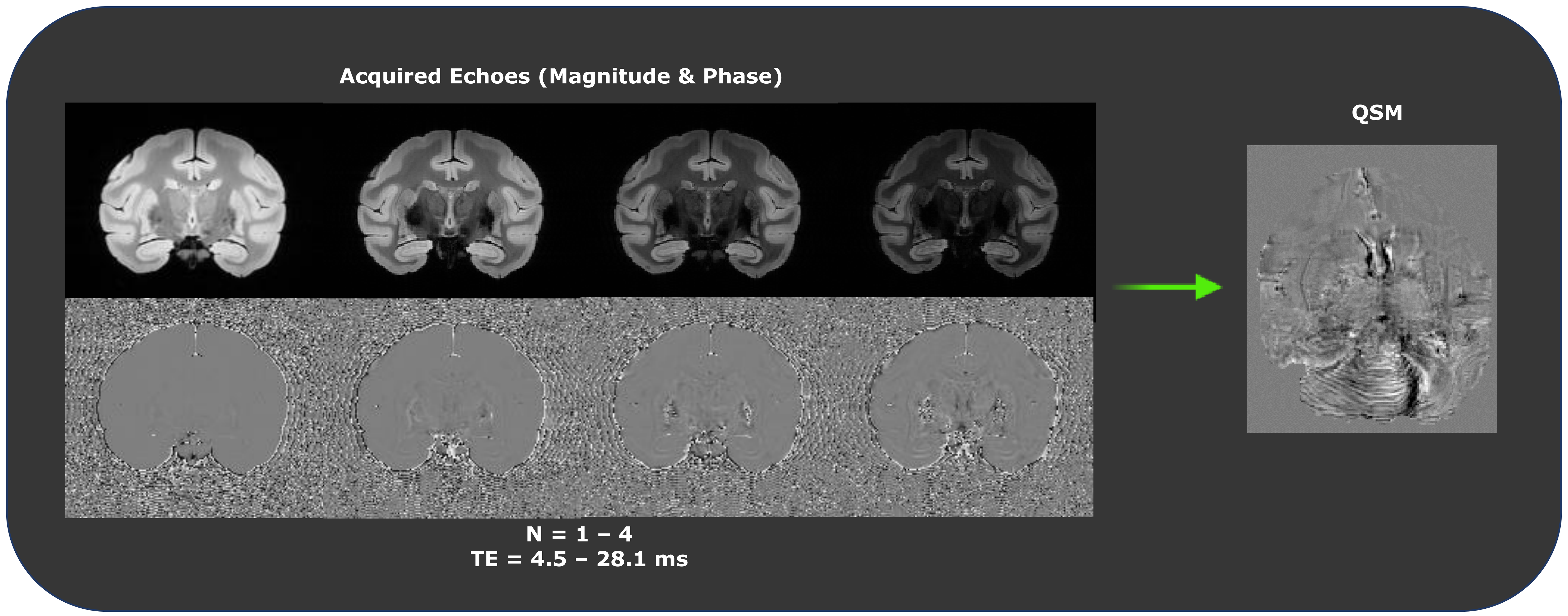
- No significant positive or negative correlations were found between our MR metrics and age using voxel-wise analysis.
- No significant positive or negative correlations were found in the hippocampus or white matter with respect to age using ROI analysis.
- **Both analyses produced consistent results with regards to aging.**

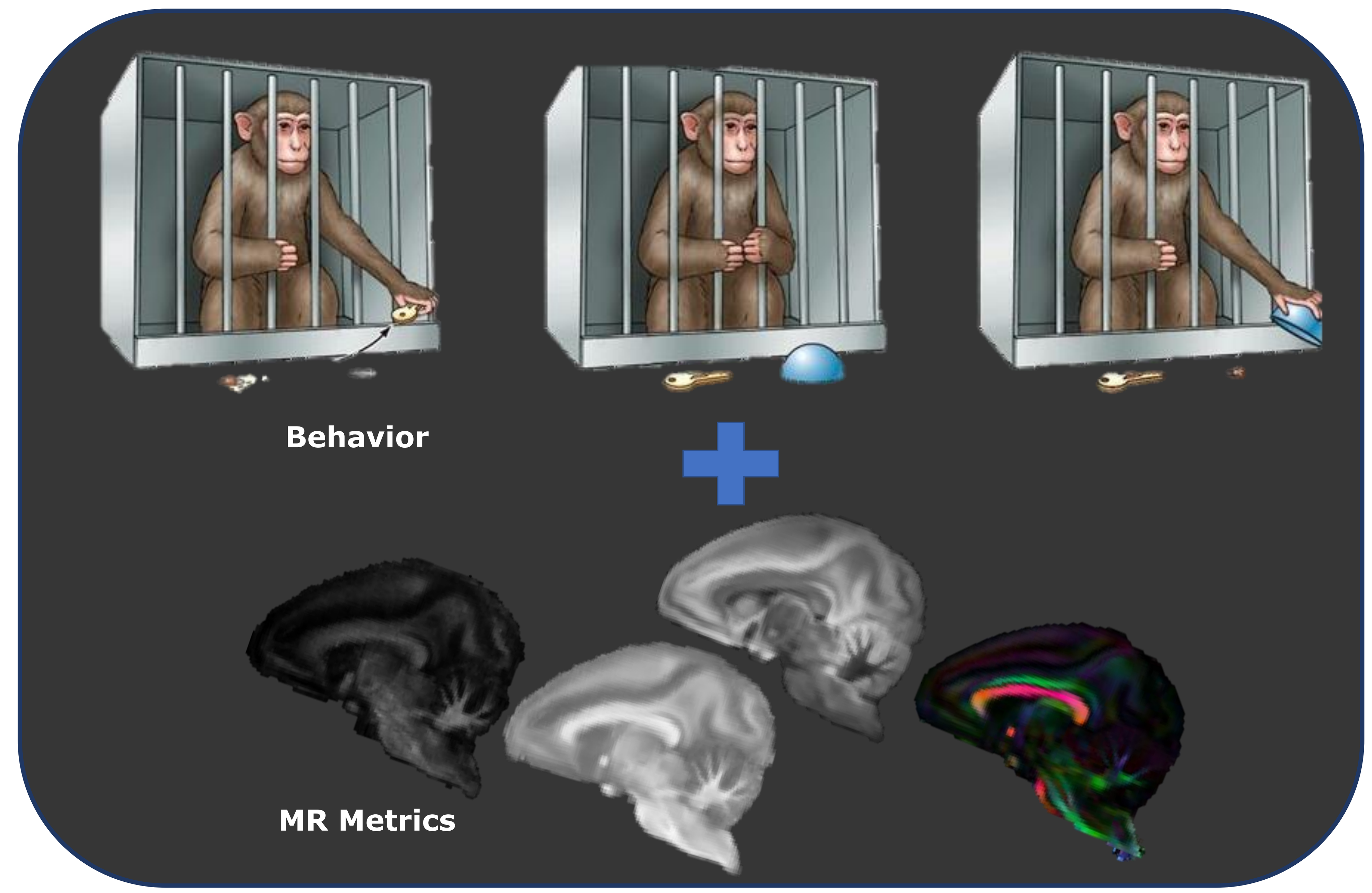
In ROI analysis with respect to MR metric correlation:

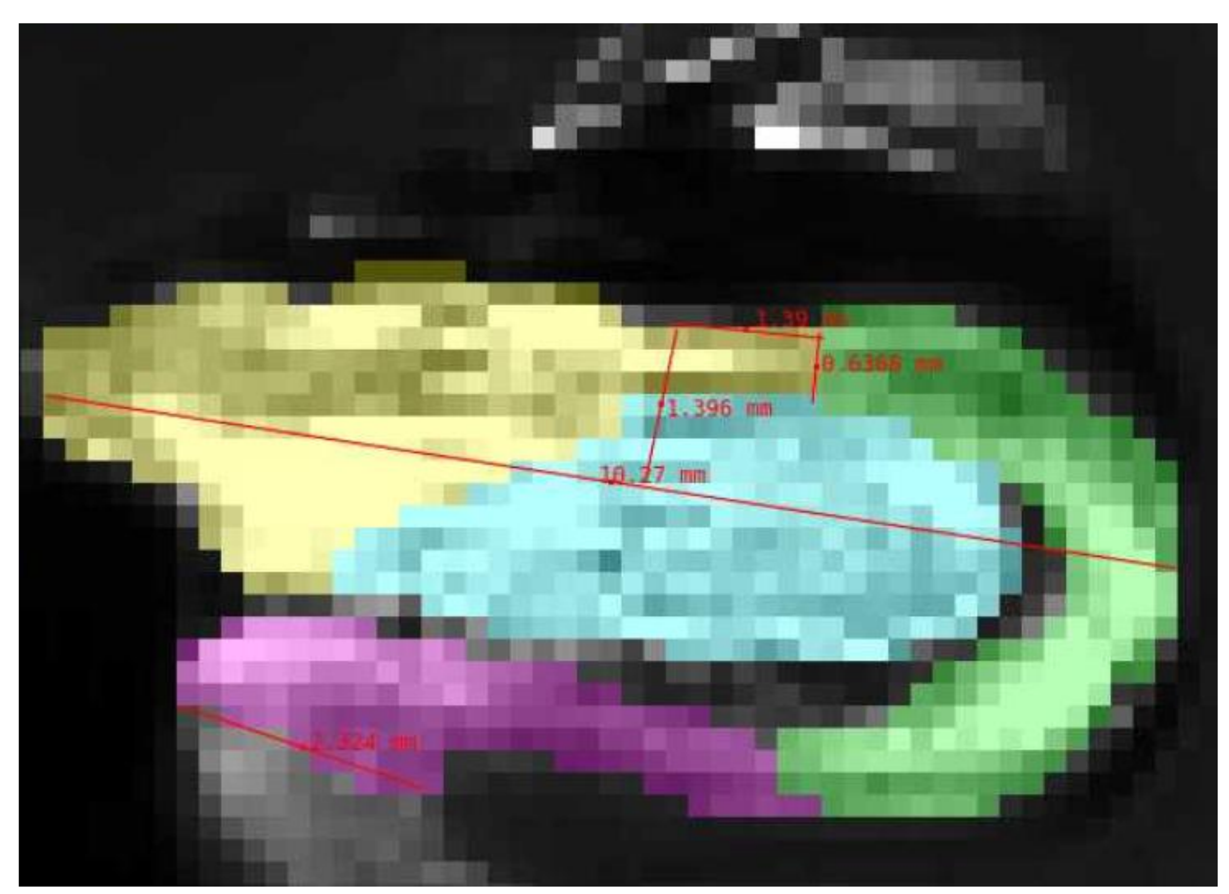
- Strong positive correlation with FA and MWF measures in white matter were observed.
- Strong positive correlation with BPF and MWF measures in the hippocampus.
- This indicates that these 3 measures, depending on location in the brain, contain similar information.
- The combination of MR metrics may be better at identifying anatomical information than a single metric on its own.

Future Directions

- Quantitative Susceptibility Maps (QSM) which is sensitive to iron and calcium accumulation.
- Voxel-wise and ROI analysis with behavioral data and age.
- Use principal component analysis to perform dimensionality reduction to test if the combination multiple MRI metrics (features) can characterize normal aging.
- ROI analysis of subfields of the hippocampus.







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