Comparative Analysis of Microstructural Features of Bonnet Macaque Hippocampal Subfields Using MRI Microscopy

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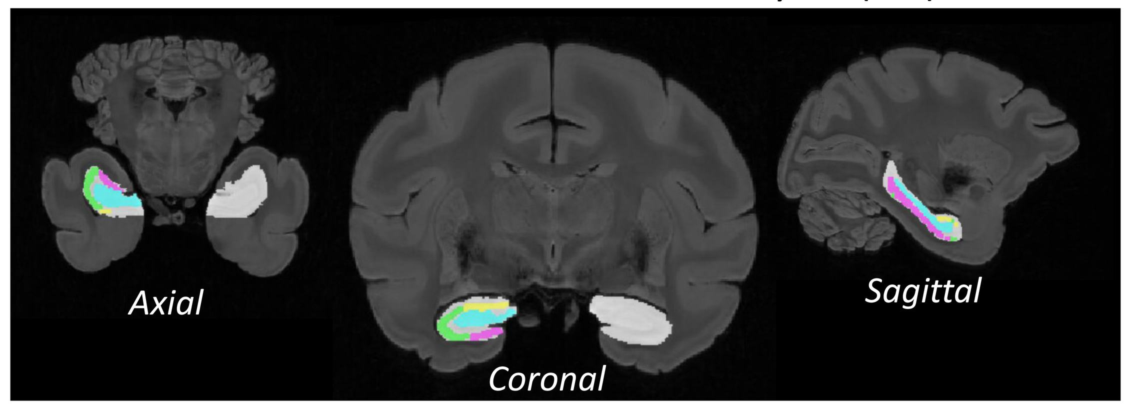
Introduction

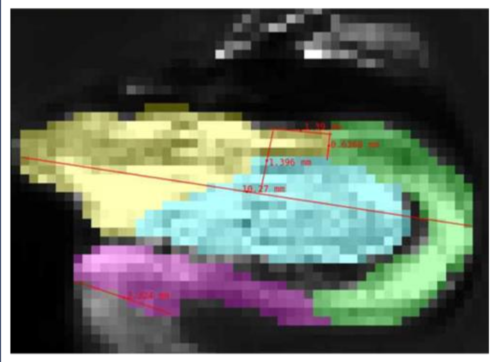
- Hippocampus subfields are highly organized.
- They contain microscale features that are detectable Magnetic Resonance Imaging (MRI) techniques.
- These differences are important when assessing structural changes that may have behavioral correlates and could be potential biomarkers for age.
- Nonhuman primates (NHPs) are an excellent animal model to investigate this region.
  - Human-similar
  - Can be validated via radiologic-pathologic studies.
- We performed high resolution *ex vivo* imaging (200 - 600 µm isotropic) on perfused whole brains of 8 behaviorally characterized female bonnet macaques. Ranged from 10 to 25 years old (30 to 75 human equivalent years).
- Multiple MRI metrics from diffusion and relaxometry offer insight into brain microstructures to quantify: Structural Integrity, Myelin, and Macromolecules.

Method/Experimental Design

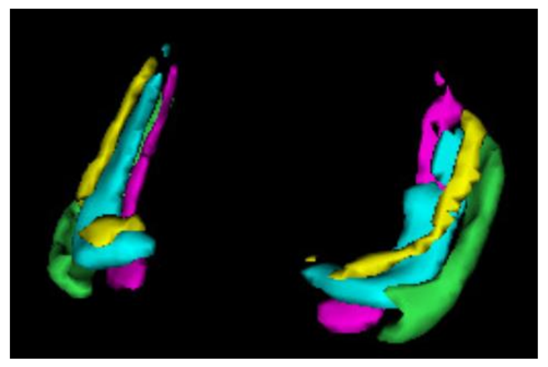
- Region of Interest (ROI) segmentation of the whole hippocampus and subfields using human protocol were drawn on high resolution anatomical (200 µm):
  - CA1,CA3, Subiculum, and Dentate Gyrus (DG)



High Resolution Anatomical with Hippocampus and Subfield Overlay

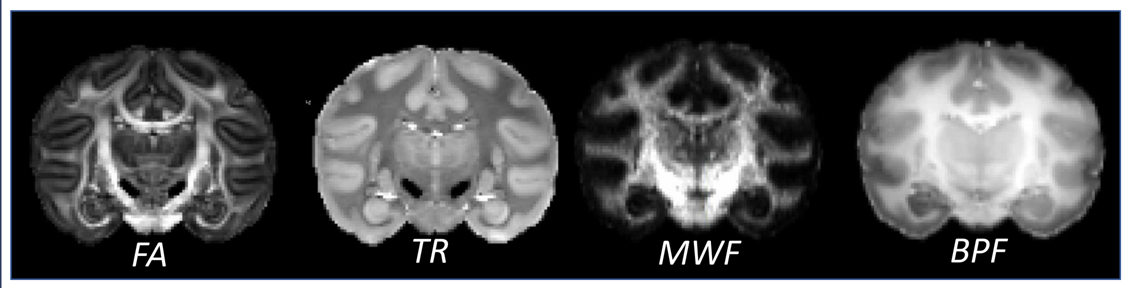


Hippocampal Subfield Protocol



3D Render of Hippocampal Subfields

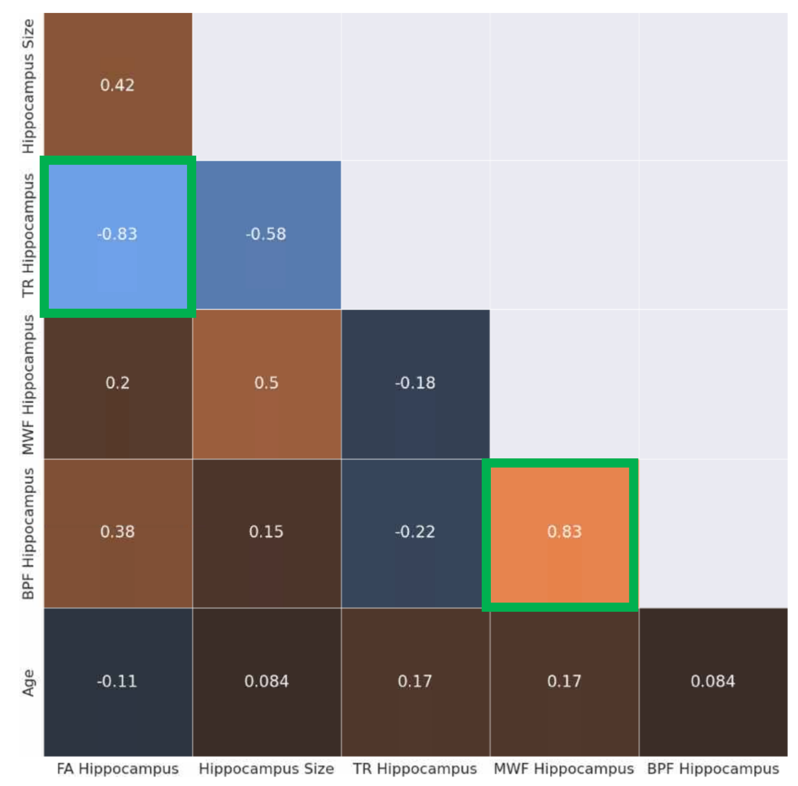
- Values were extracted on varying MR Maps:
  - Fractional Anisotropy (FA), Trace (TR), Myelin Water Fraction (MWF), Bound Pool Fraction (BPF)



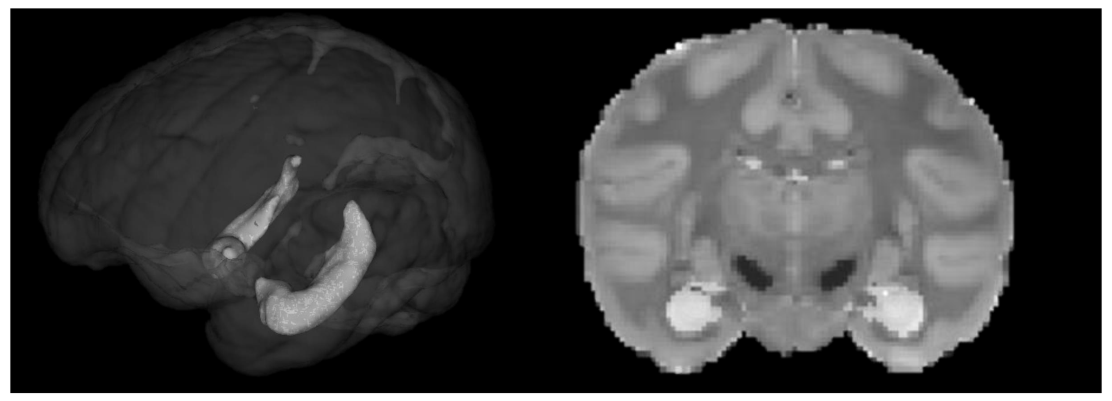
MRI Maps Assessed

- Spearman correlations were calculated and assessed for MR metrics within ROIs and age.

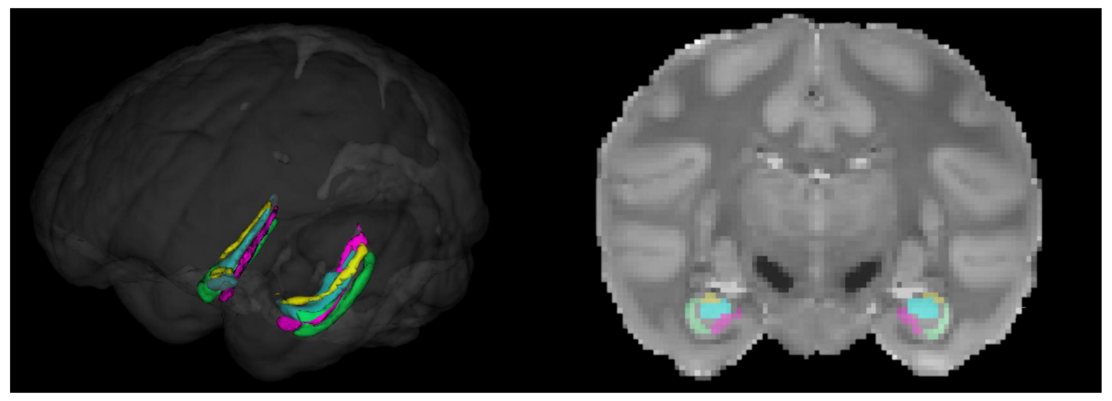
Results



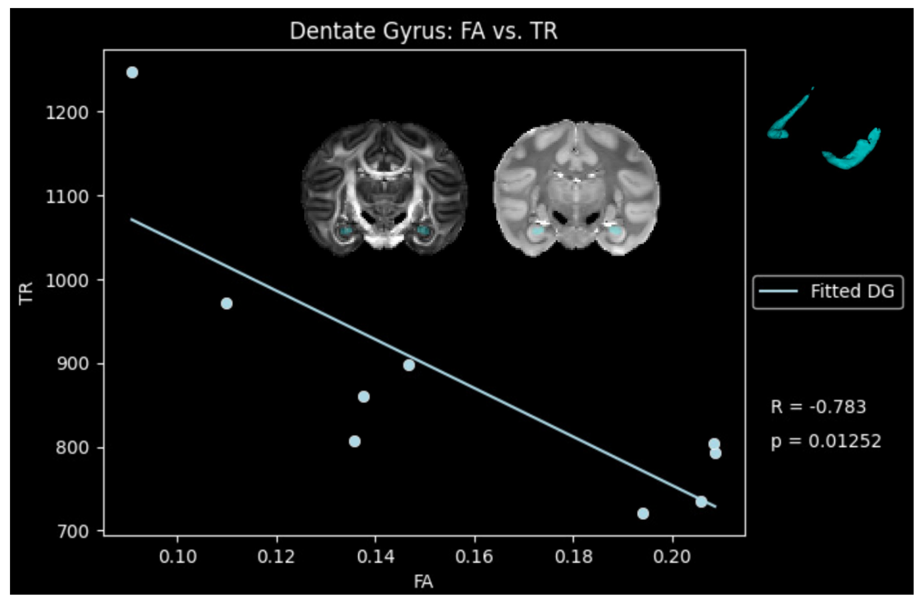
Spearman Correlation Matrix of Whole Hippocampus



Volume Render (Left) and Coronal view (Right) of the Whole Hippocampus

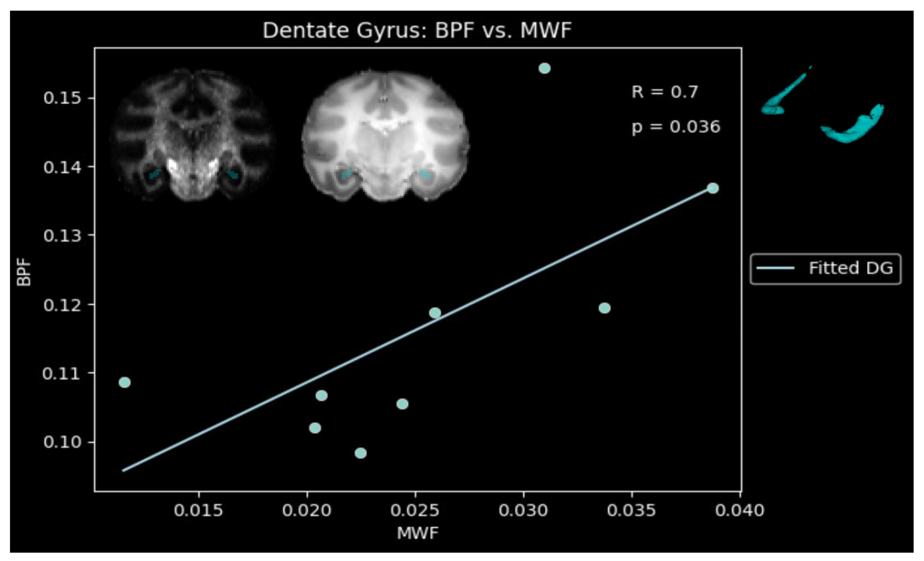


Volume Render (Left) and Coronal view (Right) of the Hippocampus Subfields

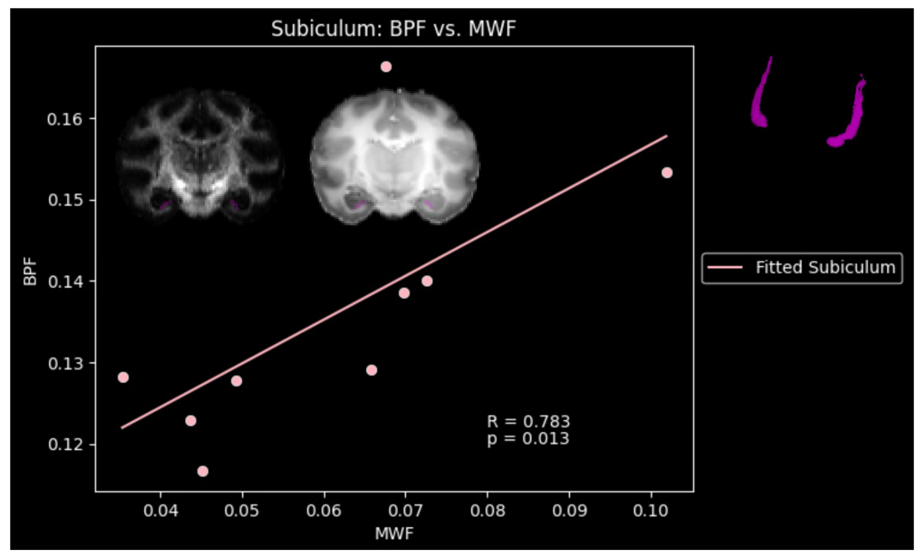


Spearman Correlation of FA vs. TR (Dentate Gyrus)

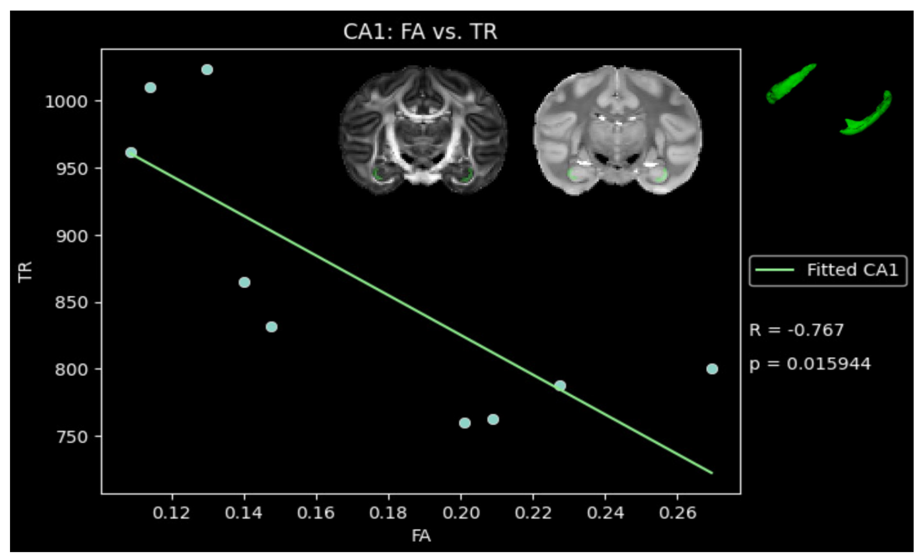
- **Whole hippocampus analysis resulted in**:
  - No correlation with age.
  - BPF and MWF positively correlated.
  - FA and TR negatively correlated.
- **Hippocampus Subfield analysis resulted in:**
  - No correlation with age.
  - FA and TR were significantly correlated in DG (R= -0.783,p= 0.012), CA1 (R= -0.767,p=0.015), CA3 (R= -0.717,p= 0.03)
  - Only 2 of the subfields had significant correlations between MWF and BPF: DG (R= 0.7,p= 0.036) and the Subiculum (R=0.783,p= 0.013).



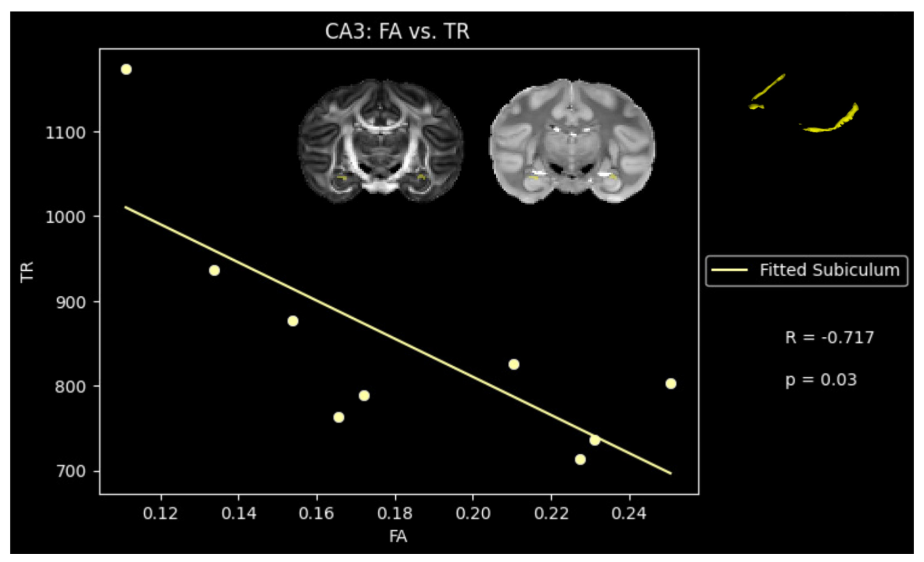
Spearman Correlation of MWF vs. BPF (Dentate Gyrus)



Spearman Correlation of MWF vs. BPF (Subiculum)



Spearman Correlation of FA vs. TR (CA1)



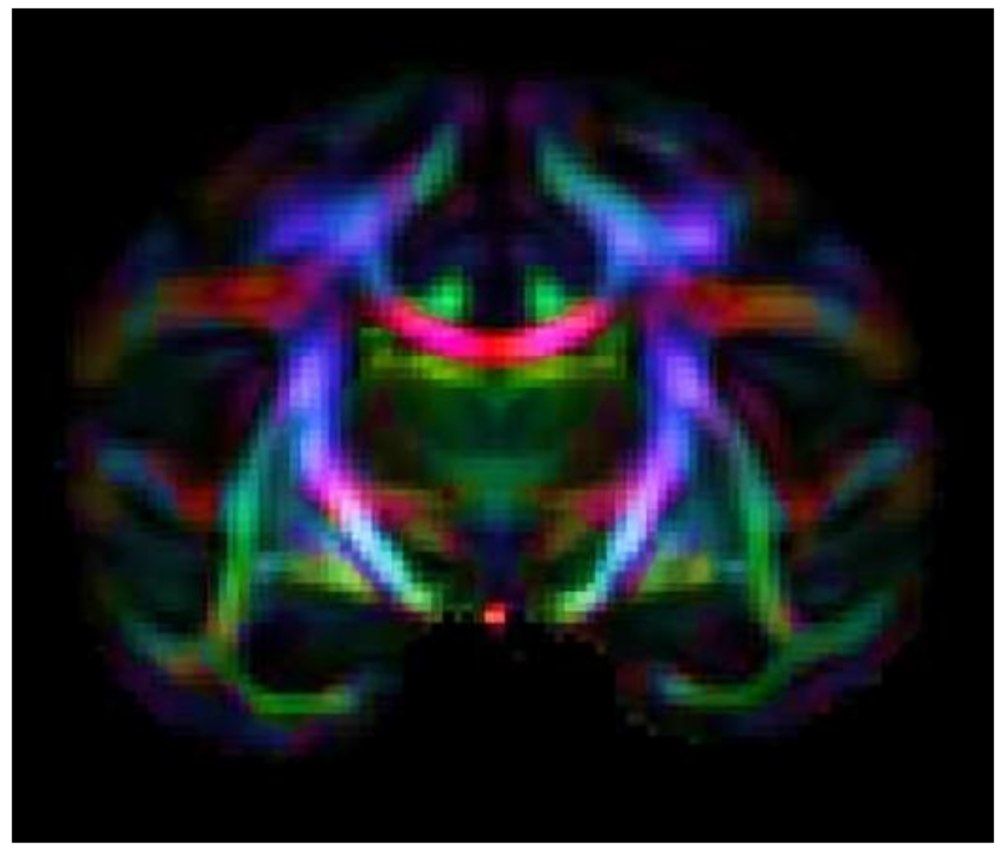
Spearman Correlation of FA vs. TR (CA3)

Conclusions

- We observed significant correlations at the whole hippocampus level:
  - MWF and BPF (R= 0.83)
  - FA and TR (R= -0.83)
- This led us to further investigate the subfields to see if there were specific regions driving this correlation.
- FA and TR were correlated in only 3 subfields (CA1, CA3,DG).
- MWF and BPF were correlated with the DG and the subicular subfields.
- These correlations have the potential offer further insight on the environmental landscape of the hippocampus that would otherwise be limited when only investigating volumetric changes or exclusively FA changes.

Future Directions

- Assessment in template space would allow:
  - Support Vector Machine Classification
  - Voxel-wise analysis
- Assessment of delineation of the subfields of the hippocampus in a less biased manner.
- Also, leveraging subfield protocol to determine if additional MR metrics (e.g MWF and BPF) offer methods of delineation of subfield microstructure.
- Has the potential to aid in automated segmentation in the future.



Diffusion Encoded Color (DEC) Map of Template

References

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