

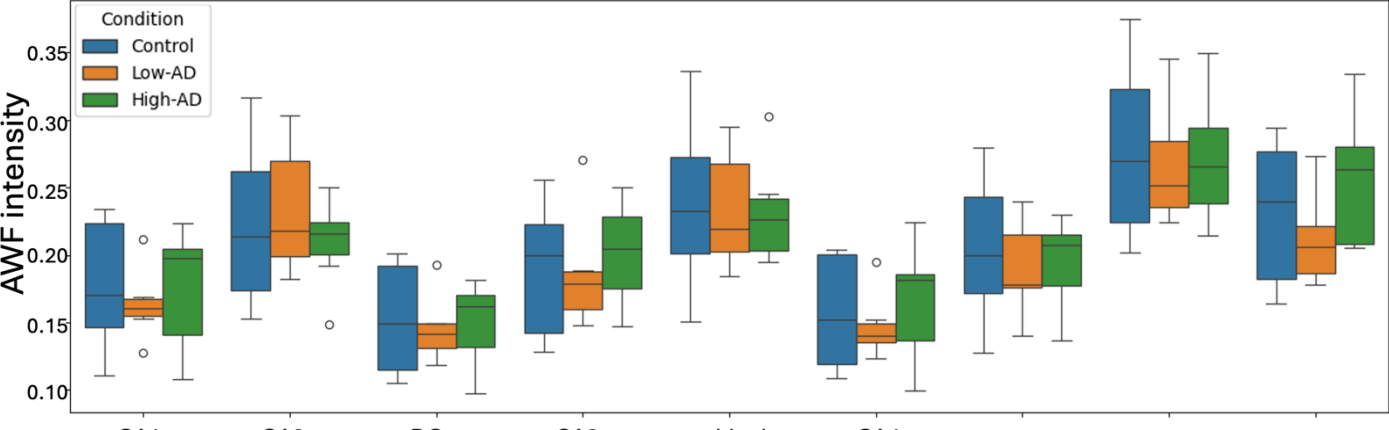
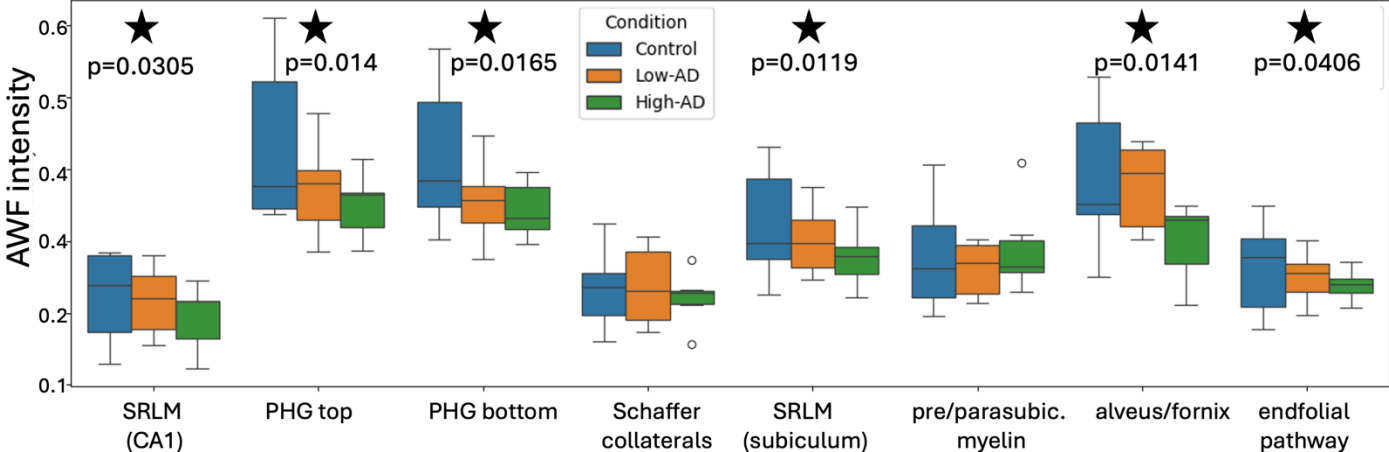
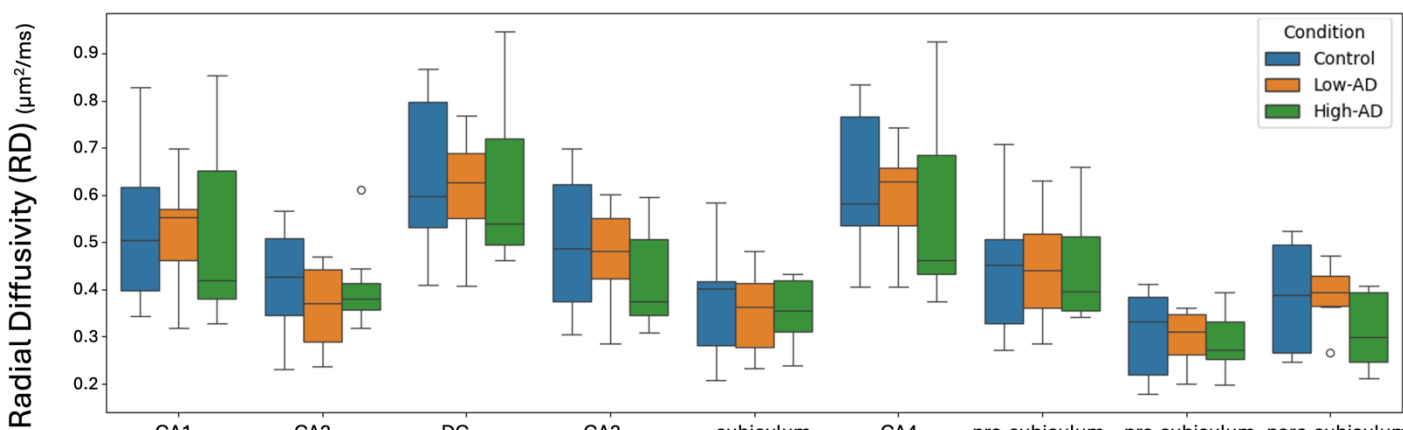
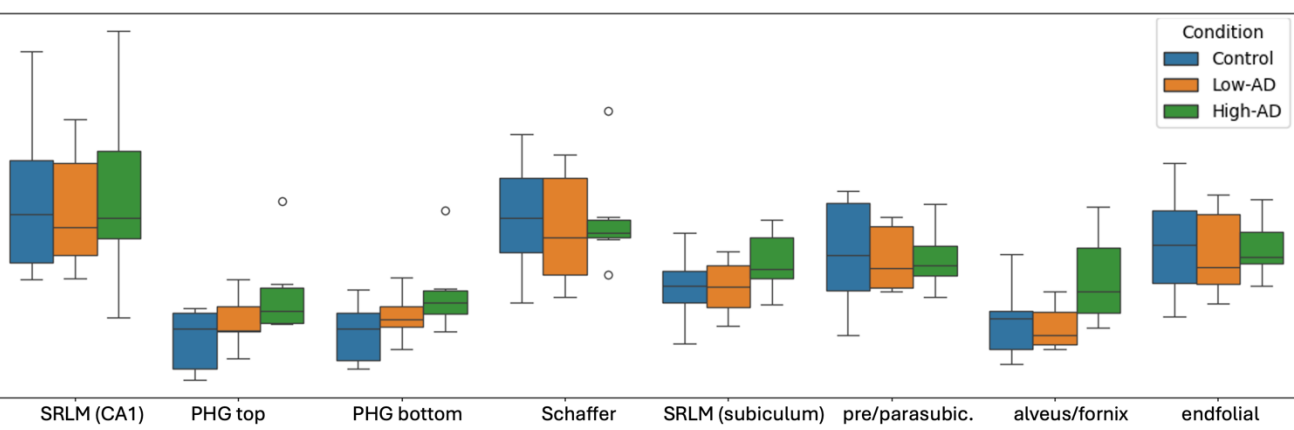
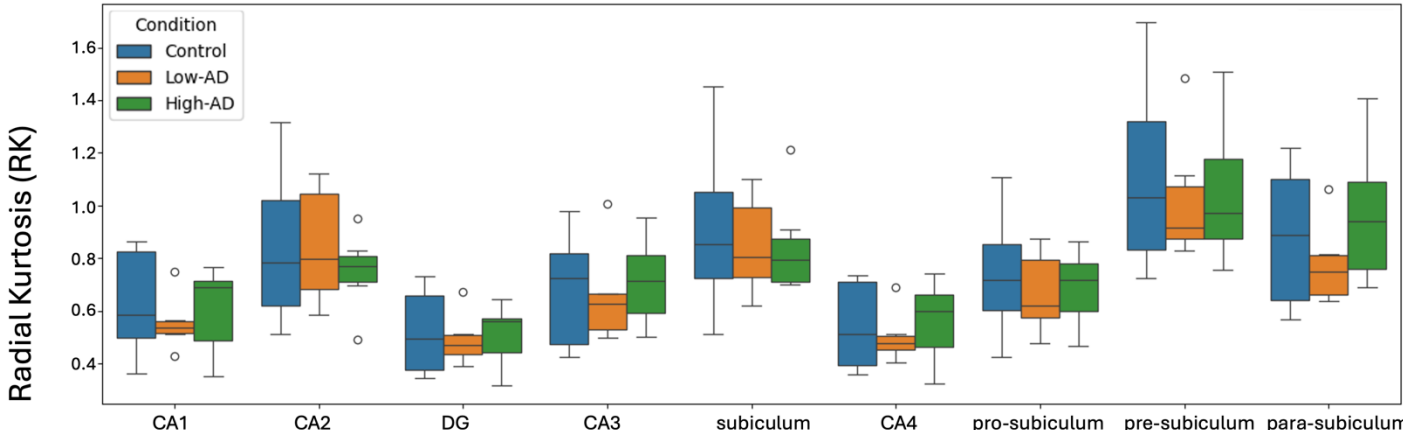
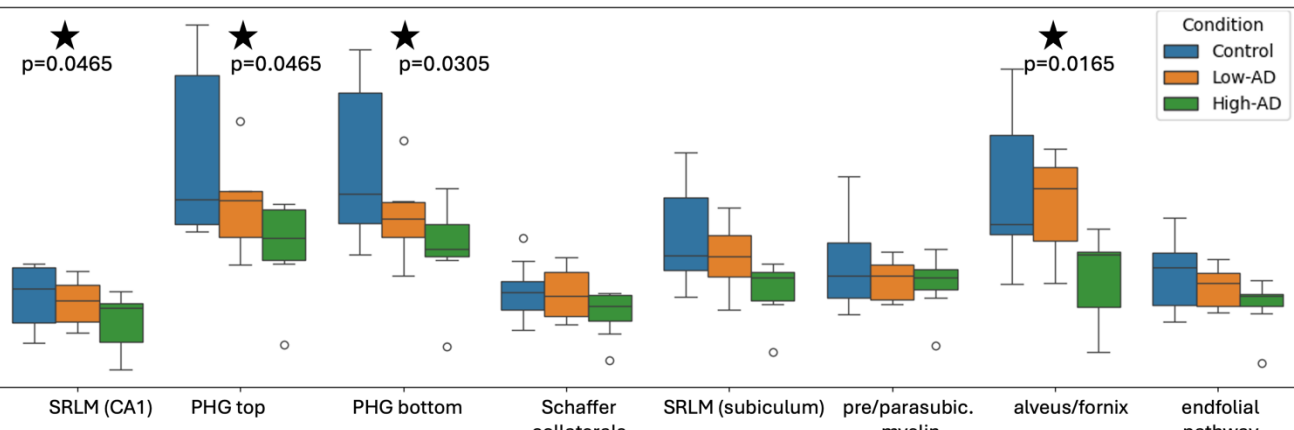
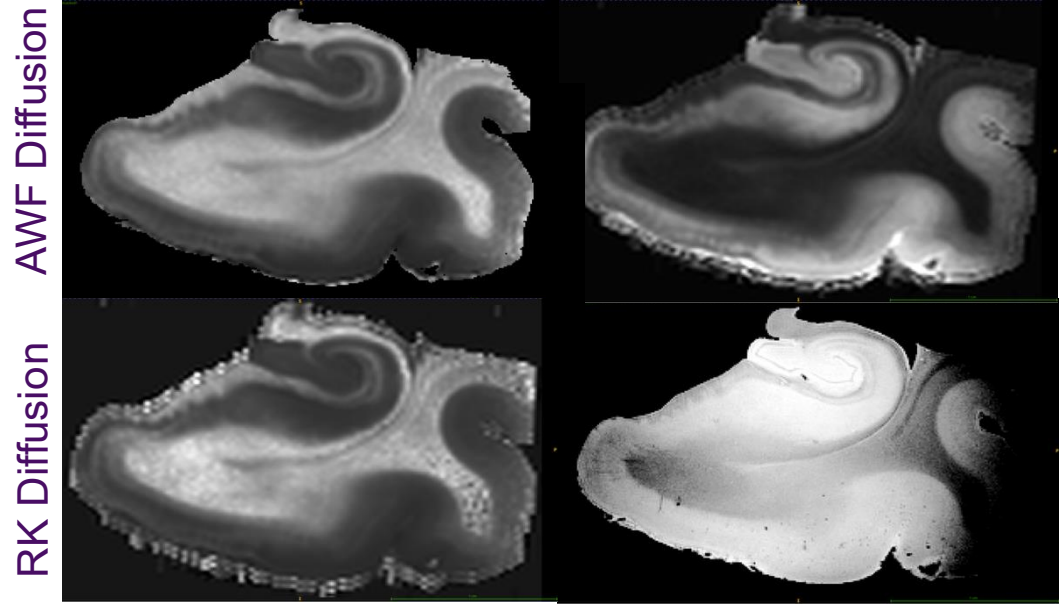
Quantifying Myelin Degeneration In Alzheimer's Disease In Human Hippocampus Subfields And Tracts Using MRI



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- Progressive myelin loss occurs in hippocampal tracts as AD worsens
- Advanced diffusion MRI can quantify these tract-specific myelin changes

INTRODUCTION		RESULTS		REFERENCES
- Myelin is a multi-layered lipid-rich sheath surrounding axons - It enables fast signal transaxion - It provides trophic support for neurons - Increasing imaging and –omic evidence implicate it in Alzheimer’s Disease - However, its role in AD remains unknown - Hippocampus is the central memory and cognition hub, severely affected by AD - Diffusion MRI is sensitive to tissue microstructure - Basic diffusion metrics, such as radial diffusivity (RD), and advanced diffusion metrics, such as axonal water fraction (AWF) and radial kurtosis (RK), can model the effect of myelin in the axons, and can be used to detect myelin changes in AD GOAL: Quantify myelin levels in hippocampal subfields and tracts for AD specimens vs controls using diffusion MRI.		Axonal water fraction (AWF) values reflected myelin levels in hippocampal subfields (top) and tracts (bottom) for Control, Low-, High-AD specimens. Subfields: Most subfields showed a V-shaped trend: control values were higher than low AD, while high AD showed higher AWF intensity than both groups.  Tracts: Most tracts showed decreased myelin levels with AD stage. Stars indicate significance in the JT test, suggesting decreasing levels with disease stage.  Subfields  Tracts  Radial Kurtosis (RK)   Radial diffusivity (RD) – top: no significant results for either subfields (left) or tracts (right) Radial kurtosis (RK) – bottom: Similar to AWF, RK had a V-shaped trend in subfields and decreased with AD stage in most tracts detected by AWF. Significance in the JT test, suggesting decreasing myelin levels with AD stage, is indicated by a star, with the (uncorrected) p-value under it.		- Ades-Aron, B. et al. Neuroimage 183, 532–543 (2018). - Dong, J. W. et al Neurobiol. Aging 89, 118–128 (2020). - Fieremans, E. et al. AJNR Am. J. Neuroradiol. 34, 2105–2112 (2013). - Georgiadis, M. et al. Nat. Commun. 12, (2021). - Georgiadis, M. et al. Nat. Commun. 16, 9572 (2025). - Insauti, R. & Amaral, D. G. Chapter 24 (eds Mai, J. K. & Paxinos, G.) 896–942 (Academic Press, San Diego, 2012). doi:10.1016/B978-0-12-374236-0.10024-0. - Mancini, M. et al eLife 9, e61523–e61523 (2020). - van Staaldunin, E. K. & Zeineh, M. Neuroimaging Anat. Part 1 Brain Skull 32, 475–489 (2022). - Wang, Q. et al NeuroImage Clin. 22, 101767 (2019). - West, M. J., Coleman, P. D., Flood, D. G. & Troncoso, J. C Lancet Lond. Engl. 344, 769–772 (1994). - Yushkevich, P. A. et al. Brain J. Neurol. 144, 2784–2797 (2021). - Zeineh, M. M. et al.. Cereb Cortex 27, 1779–1794 (2017). - Zeineh, M. M., Engel, S. A., Thompson, P. M. & Bookheimer, S. Y Science 299, 577–580 (2003).
METHODS		CONCLUSIONS		CONTACT
21 fixed hippocampi (8 control/6 Low- /7 High-AD) scanned at Bruker 7T - Diffusion-MRI (100 directions at b=[1,2,5,10]ms/μm, 200μm iso) - Multi-gradient echo (MGE) (10 echoes, TE=4-40ms, 100μm iso) - Diffusion metrics reflecting myelin levels (radial diffusivity-RD, radial kurtosis-RK, axonal water fraction-AWF) were generated using DESIGNER  - Aligned MGE and diffusion MRIs to improve segmentation accuracy - Followed a rule-based system of anatomic and myelin-based images, atlases, and landmarks		- We studied myelin levels in hippocampal subfields and tracts in Control, Low- and High-AD specimens using advanced diffusion-MRI metrics - Advanced metrics (AWF, RK) were more sensitive in detecting changes than basic ones (RD) - Tracts: AWF levels significantly decreased with AD status in most tracts, showing a linear drop or a drop in high AD, except alveus/fornix. This might be reflecting the myelin degeneration increasingly implicated in AD - Subfields: Most subfields exhibited a V-shape trend, with AWF levels decreasing in Low-AD and increasing in High-AD (either bouncing back or overshooting) - This could reflect a compensatory mechanism following hippocampal neurodegeneration - Overall, we showed that diffusion MRI metrics can be used to assess myelin levels, revealing important localized trends in myelin degeneration in AD in the human hippocampus Future work: - Validating results with myelin-specific methods (X-ray scattering) - Identifying proteomic, lipidomic, and transcriptomic signatures of changes - Correlating with amyloid/tau - Combine with microscopic tract delineation and degeneration using micron-resolution methods		Vivian Zhu - vivianzh@stanford.edu Marios Georgiadis - mariosg@stanford.edu Michael Zeineh – mzeineh@stanford.edu Stanford University – Zeineh Lab