

Predicting Tau Positivity Using Gray Matter Diffusion Weighted Imaging

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Introduction

- Alzheimer's disease (AD) is highly prevalent in older adults and is the leading cause of dementia worldwide. Its prevalence is projected to rise significantly as the global population continues to age.¹
- AD is primarily characterized by two pathologies: amyloid- β plaques and tau neurofibrillary tangles.
 - The established pattern of tau spread begins in the transentorhinal cortex, throughout the limbic cortex, and finally extends into neocortical regions.²
- Currently, the most reliable way to detect tau in vivo is using a PET scan, which can be expensive and inaccessible.
- Previous studies have used structural MRI measures (e.g., brain volume and cortical thickness) as well as diffusion-weighted imaging (DWI) of white matter to predict tau positivity.^{3,4,5}

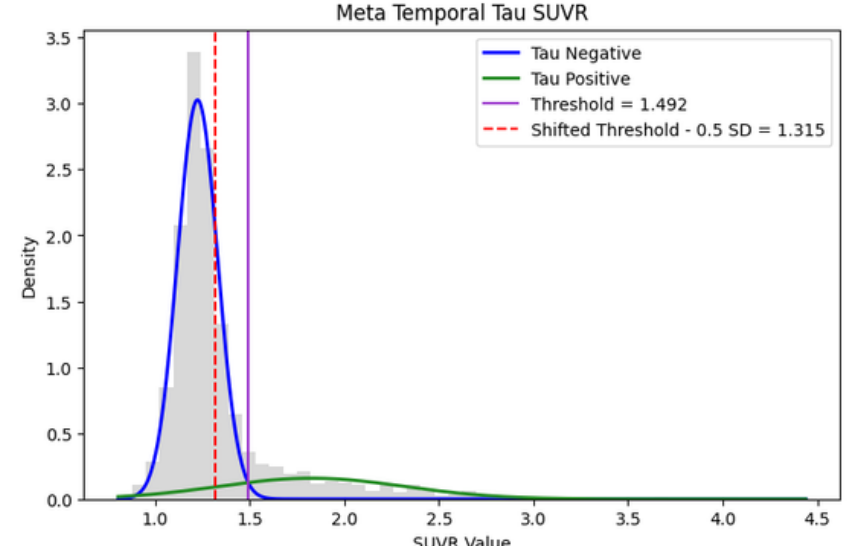
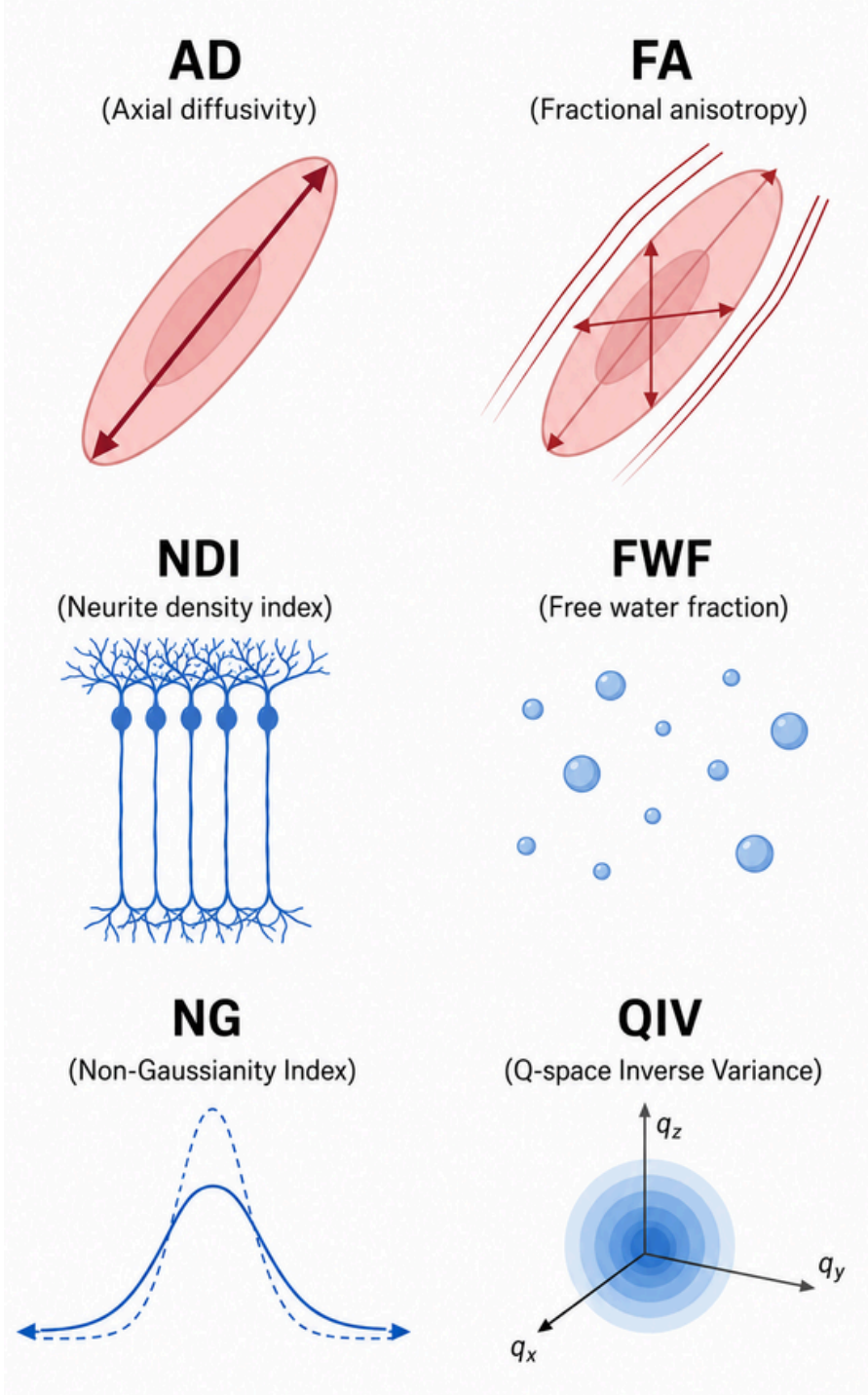
Objective: to characterize tau positivity using gray matter DWI measures, with a particular focus on temporal lobe regions.

Methods

Demographics

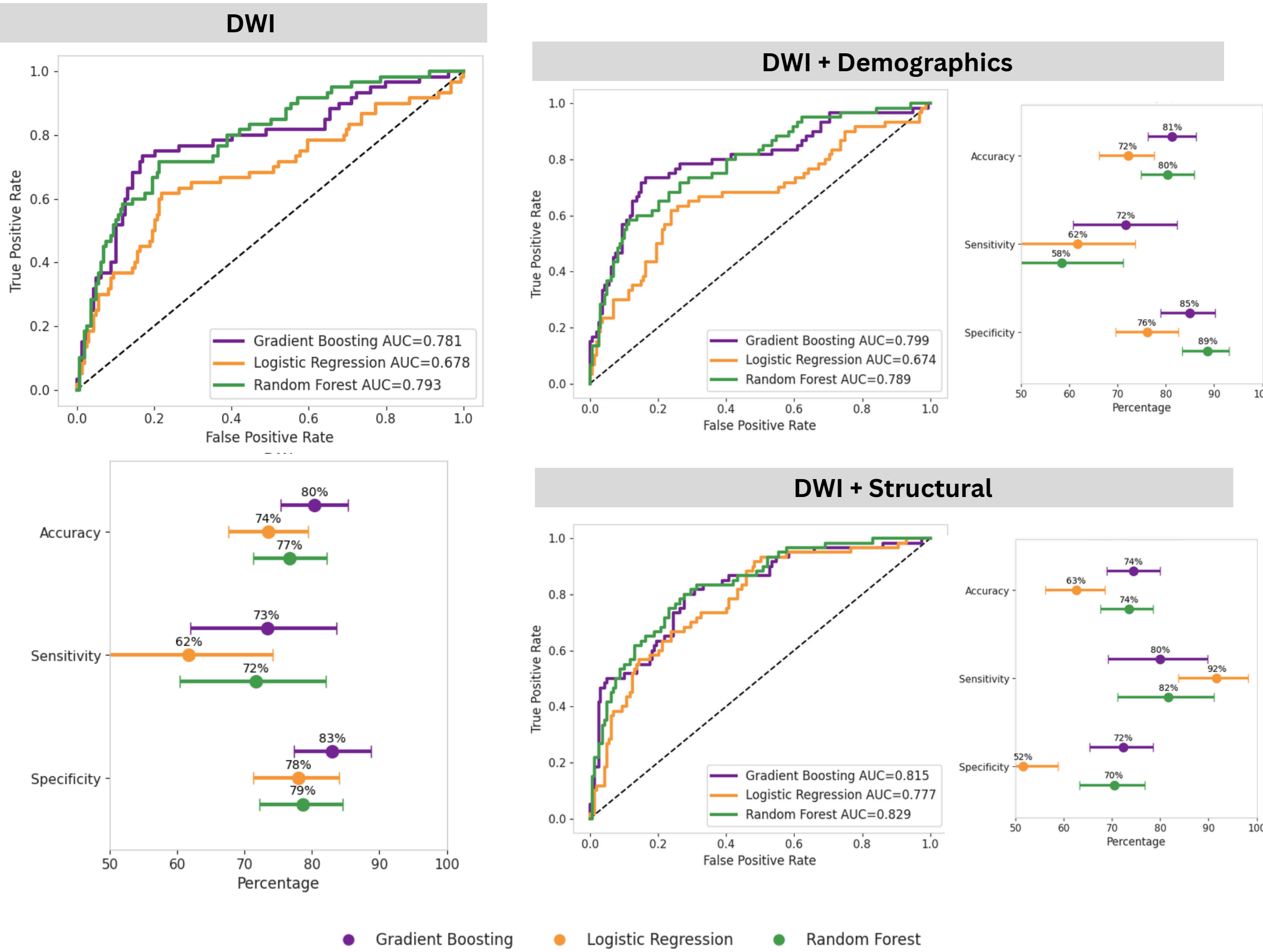
Study	Age (years)	Sex (% female)	Cognitive Impairment	% Tau Positive
ADNI (n = 141)	77.5 $\pm$ 7.6	58.9%	43.3% CI	15.6%
SCAN (n = 75)	72.4 $\pm$ 7.7	41.3%	78.7% CI	49.3%

Processing/Analysis



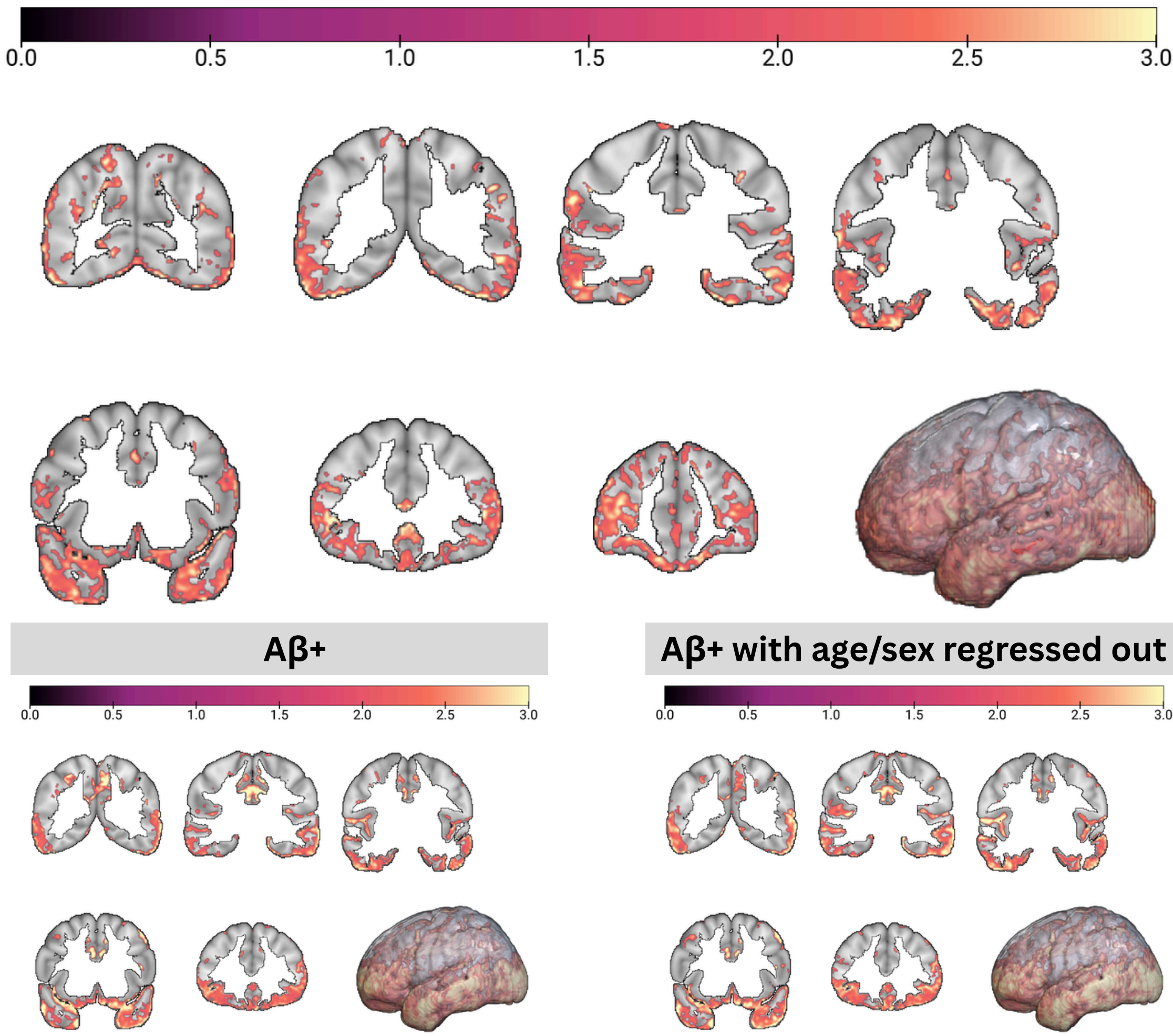
- Established tau positivity threshold using a Gaussian mixture model.
- Machine learning classification:
 - 5 fold CV using combinations of DWI, demographics, and structural MRI
 - Gradient boosting
 - Logistic regression
 - Random forest
- Voxelwise analysis:
 - Support vector machine (SVM) implemented in Nilearn
 - Combined all DWI metrics as input features
- Regional SUVR analysis:
 - Used non-linear ensemble with DWI inputs to predict continuous tau PET SUVR values
 - Structural measures added to further improve prediction

DWI and Structural MRI Predict Tau Positivity



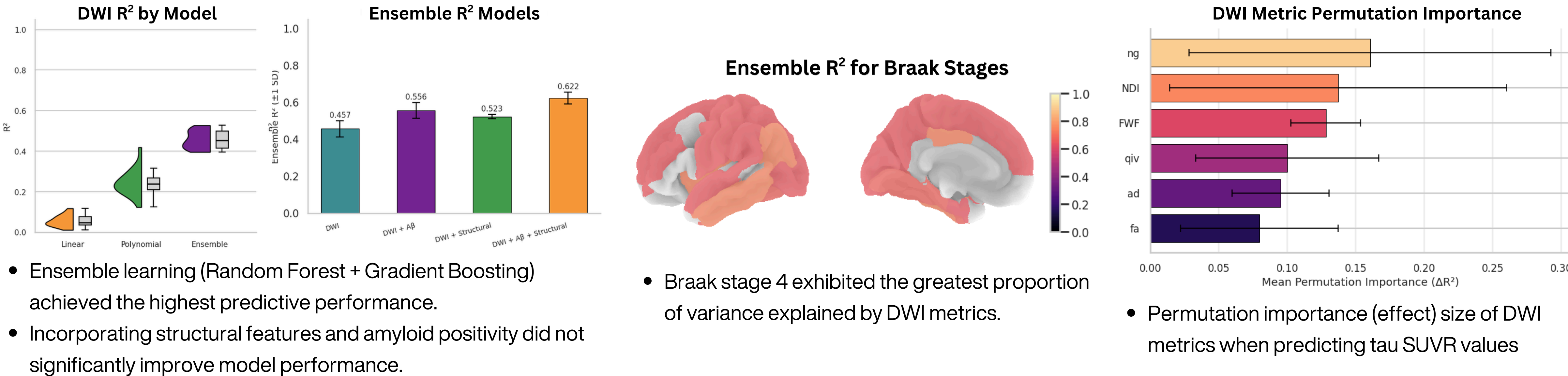
- DWI is a strong predictor of tau positivity status.
- Nonlinear models (gradient boosting, random forest) outperform logistic regression.
- Structural MRI improves AUC and sensitivity; demographics provide minimal added value.

Voxelwise DWI Predicts Positivity Consistent with Tau Spread



- Z-statistic map Fisher-transformed from voxel correlation to SVM decision scores, where a higher absolute value means that voxel is more predictive of tau positivity.

Ensemble Learning Supports Reliable Regional Tau SUVR Prediction



- Ensemble learning (Random Forest + Gradient Boosting) achieved the highest predictive performance.
- Incorporating structural features and amyloid positivity did not significantly improve model performance.

- Braak stage 4 exhibited the greatest proportion of variance explained by DWI metrics.

- Permutation importance (effect) size of DWI metrics when predicting tau SUVR values

Discussion

- Gray matter diffusion metrics accurately classify tau positivity.
- The temporal lobe appears to be a prominent area affected during tau accumulation, showing altered diffusion consistent with Braak stage accumulation.
- Temporal lobe gray matter DWI could be a promising predictor of tau positivity, potentially reflecting microstructural differences or neurodegeneration associated with tau accumulation.
- Future directions will investigate neocortical tau positivity patterns and mapping that using DWI.

References

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