

Background

- Recent advancements in deep learning enabled leveraging large-scale neuroimaging data to predict disease-related outcomes, such as Alzheimer's disease (AD) risk and clinical staging.
- Prior classification studies have largely used data from T1-weighted structural magnetic resonance imaging (MRI) and conventional diffusion MRI (dMRI). Incorporating free-water (FW) imaging may improve the biological specificity of models.
- The goals of the present study are:
 - To build residual network (ResNet) classifiers of AD clinical staging using T1-weighted MRI, FW-corrected dMRI, and both T1 and FW images.
 - To generate model-derived probability scores for MCI individuals using all models and to evaluate their associations with memory.

Participant Characteristics & Methods

- Training/validation data were drawn from the Alzheimer's Disease Neuroimaging Initiative (ADNI, N=990); test data were drawn from the National Alzheimer's Coordinating Center (NACC, N=523). Both datasets included baseline visit of participants with cognitively unimpaired (CU), MCI, or AD status. See **Table 1** for cohort demographic and clinical information.

Table 1. Demographic and health characteristics of training/validation and test sets.

Characteristic	Training/Validation: ADNI				Test: NACC			
	CU (N=545)	MCI (N=349)	AD (N=96)	Total (N=990)	CU (N=399)	MCI (N=78)	AD (N=46)	Total (N=523)
% Female	60.0	46.1	43.8	53.5	66.3	38.5	47.8	60.6
% Non-Hispanic White	91.9	93.4	97.9	93.0	99.0	93.6	100.0	98.3
Age (years)	71.7 (7.83)	74.0 (7.79)	75.8 (8.12)	72.9 (7.97)	66.1 (11.5)	74.1 (8.21)	72.4 (10.5)	67.8 (11.4)
Education (years)	16.7 (2.29)	16.2 (2.60)	15.4 (2.43)	16.4 (2.45)	16.2 (2.49)	15.8 (2.79)	14.7 (2.75)	16.0 (2.59)

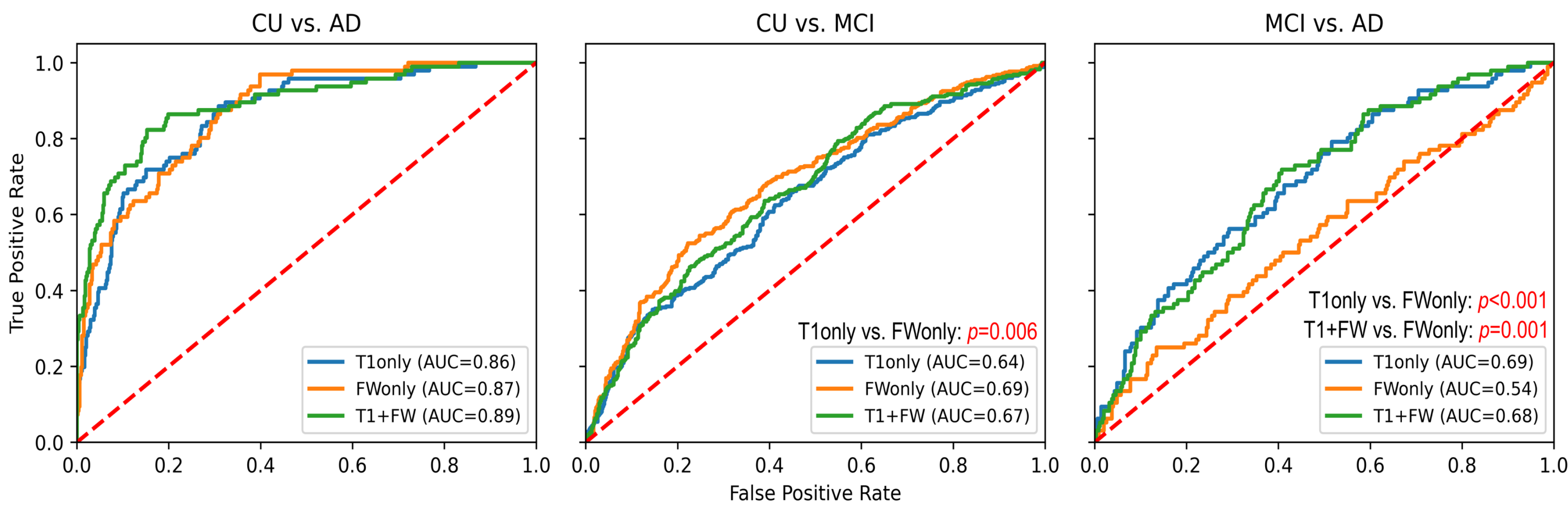
- 3D T1 and dMRI data were obtained for each participant; dMRI data underwent *PreQual* preprocessing followed by FW correction.

- Model architecture adapted the ResNet10 backbone¹ to classify AD clinical staging, optimizing on binary cross-entropy loss.
- 9 models were created from combining different input features (T1-only, FW-only, T1+FW) and classification tasks (CU vs. AD, CU vs. MCI, MCI vs. AD).
- Performance was evaluated using accuracy and area under the receiver operating characteristic curve (ROC-AUC) across 5-fold cross validation.
- Trained CU vs. MCI models were used to generate probability scores on NACC participants with cognitive data. Logit transformation² was applied to raw probability scores prior to statistical analysis.
- Main effects of logit-transformed probability scores on **cross-sectional and longitudinal memory** were assessed using a general linear model. Covariates included sex, ethnicity, age, and education.

Figure 1: CU vs. AD models showed best performance in distinguishing AD diagnostic categories.

FW-only model outperformed the T1-only model in **CU vs. MCI** classification but showed the worst performance in **MCI vs. AD** classification.

A. Receiver operating characteristic (ROC) curves for pooled out-of-fold validation samples in ADNI



B. Precision-recall (PR) curves for pooled out-of-fold validation samples in ADNI

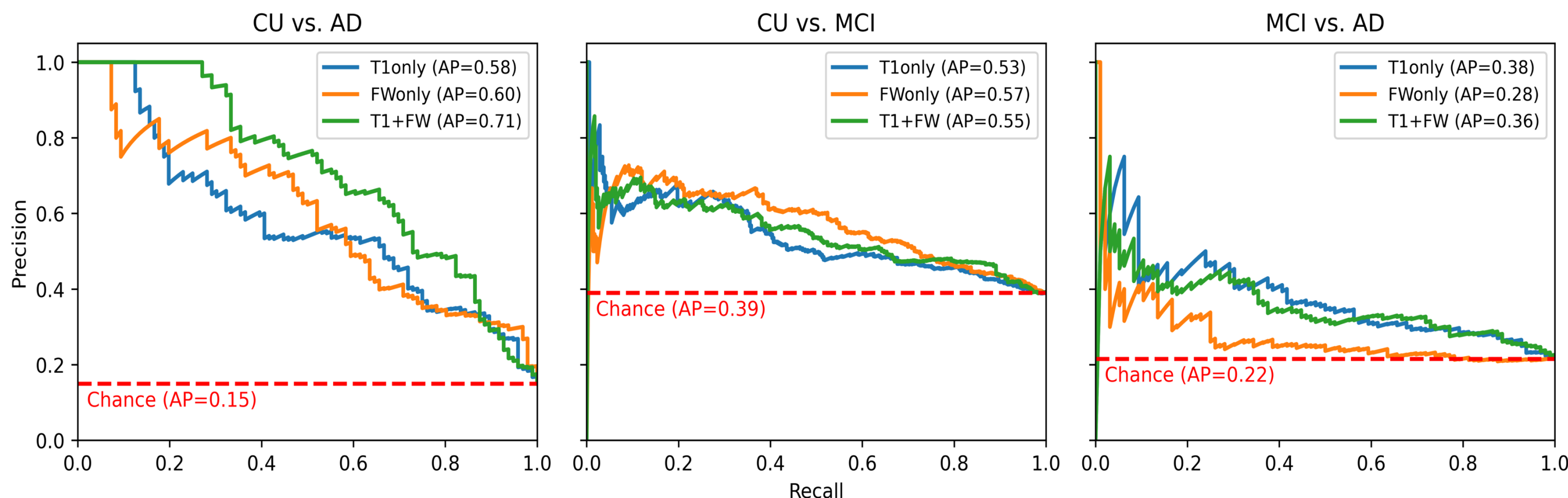
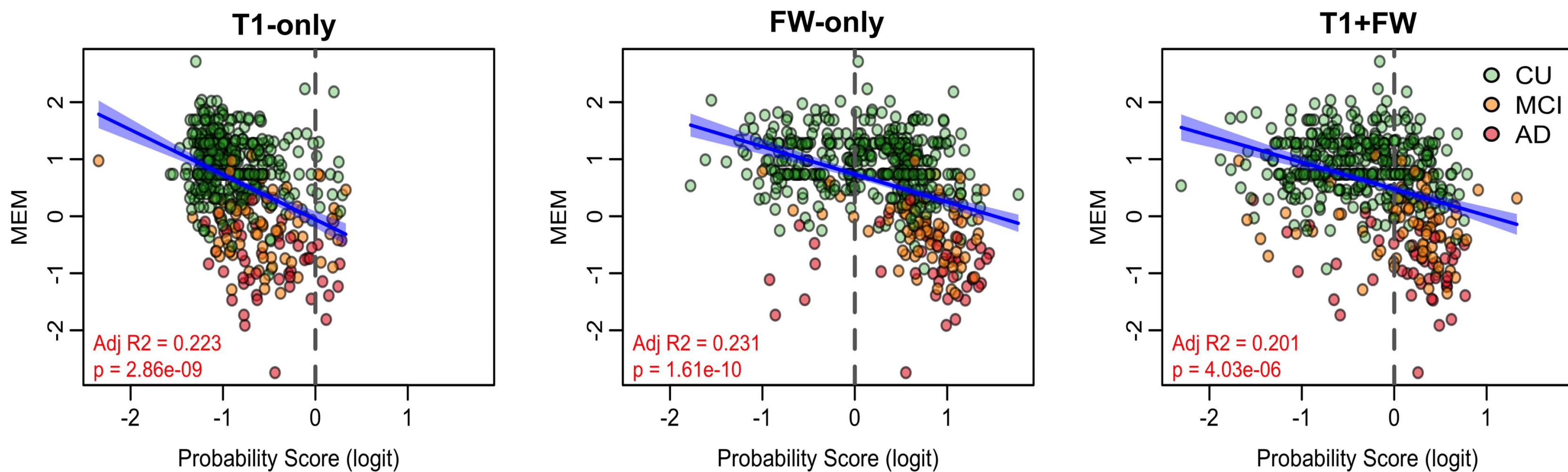
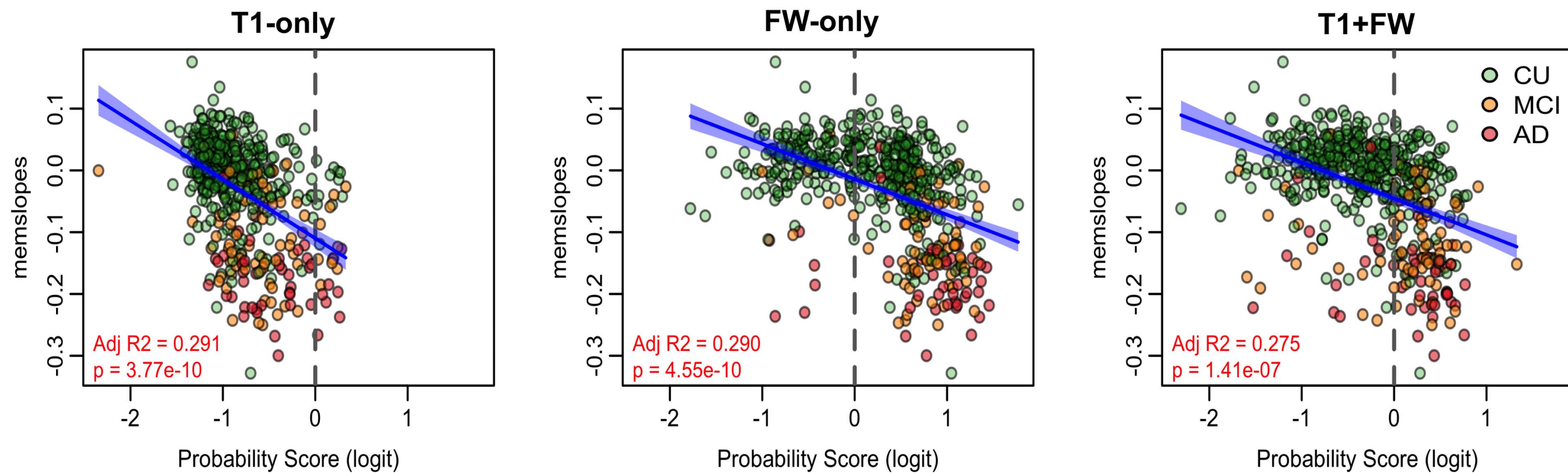


Figure 2: In CU vs. MCI models, **FW-only scores** most strongly correlated with **cross-sectional memory performance**; **T1-only scores** most strongly correlated with **longitudinal memory decline**.

A. CU vs. MCI model-generated probability score association with memory performance



B. CU vs. MCI model-generated probability score association with memory decline



Conclusions & Future Directions

Our findings suggest that free water imaging better informs CU vs. MCI classification whereas T1-informed models better distinguish MCI vs. AD categories. CU vs. MCI probability scores are associated with both cross-sectional and longitudinal memory beyond standard covariates in an independent dataset.

Future work will examine the relationship between model-derived probability scores and both cross-sectional performance and longitudinal cognitive decline in executive functioning and language domains.

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References:

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- Lesaffre, E., Rizopoulos, D. & Tsonaka, R. The logistic transform for bounded outcome scores. *Biostatistics* 8, 72–85 (2007).

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