

Whole-Brain MRI Modeling Explains Neuropsychiatric Symptom Severity Beyond Alzheimer’s Disease Stage



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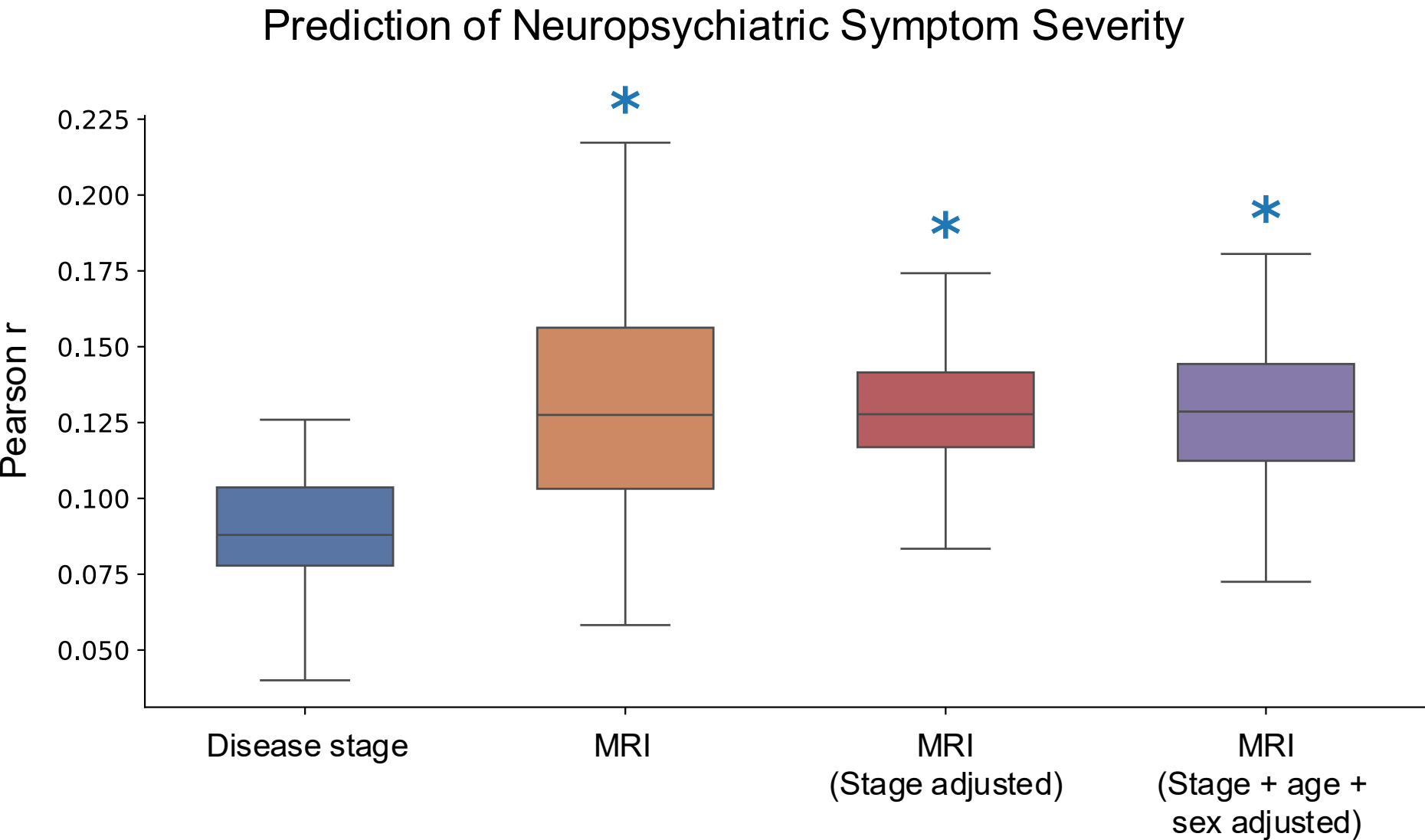
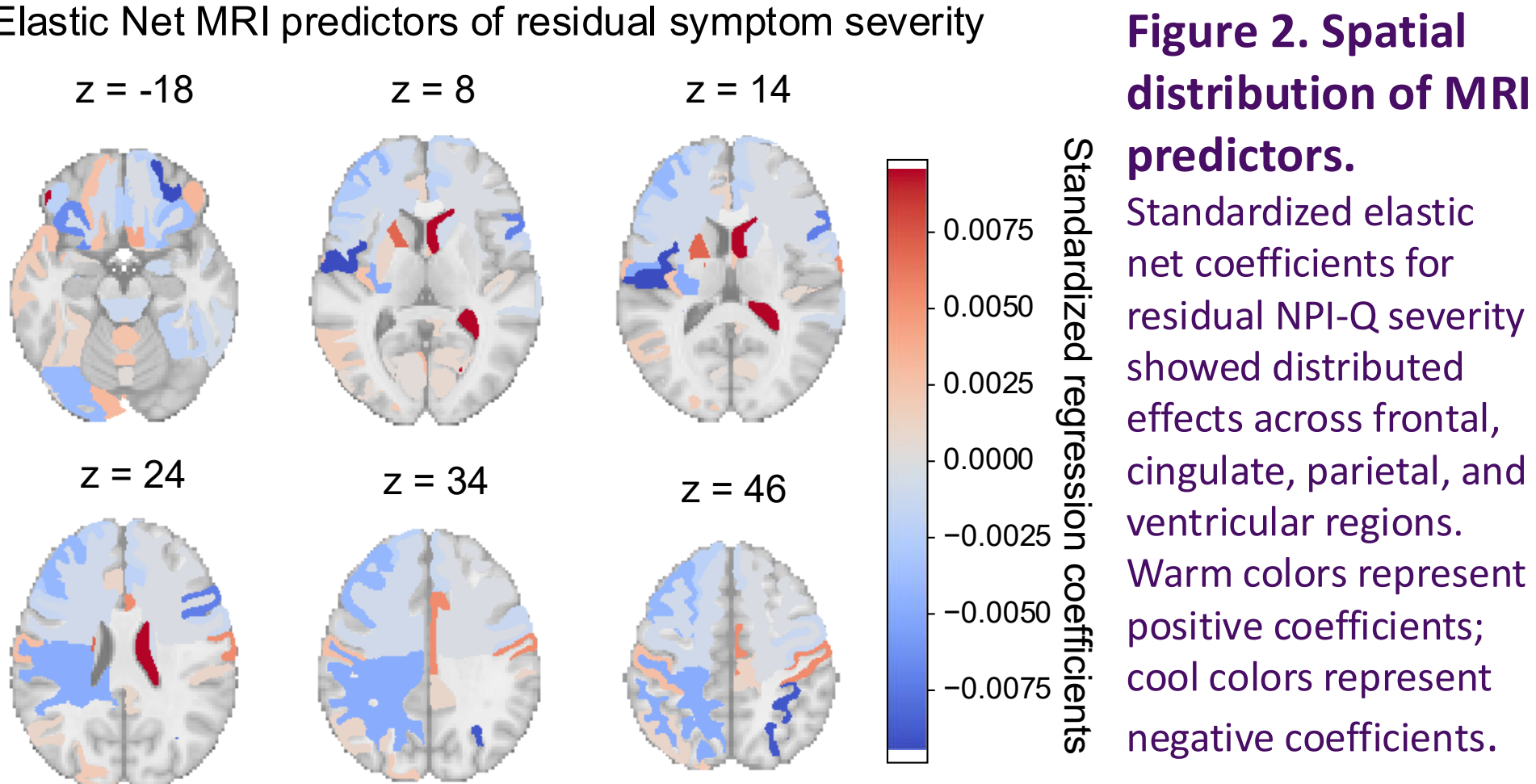
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Neuropsychiatric symptom severity in AD/MCI is better explained by distributed brain structure than by diagnosis alone.			
INTRODUCTION	METHODS	RESULTS	CONCLUSIONS
Why this matters - Neuropsychiatric symptoms are common across the Alzheimer’s disease spectrum and are linked to functional decline, caregiver burden, and poorer quality of life. - Symptom severity varies widely among individuals with similar AD/MCI diagnoses. - This heterogeneity suggests that diagnosis alone may not capture the neurobiological basis of symptom burden. Hypothesis Distributed structural MRI patterns explain NPI-Q severity beyond disease stage and demographics.	Cohort - ADNI-2 baseline T1 MRI + NPI-Q - Symptomatic AD/MCI participants: NPI-Q > 0 - Groups: AD n = 109, EMCI n = 98, LMCI n = 109 - Total: N = 316 MRI features 145 whole-brain regional volumes - Multi-atlas segmentation framework Modeling - Outcome: log-transformed NPI-Q total score - Model: elastic net regression - Validation: 10-fold CV × 100 repetitions - Comparison: diagnosis/stage one-hot model - Covariate-adjusted analysis: residualized NPI-Q for diagnosis, age, sex	Prediction of Neuropsychiatric Symptom Severity  Elastic Net MRI predictors of residual symptom severity  Figure 1. Prediction performance across repeated cross-validation. Whole-brain MRI models showed higher cross-validated Pearson correlations than disease stage alone, including after adjustment for disease stage, age, and sex. * p < 0.001 vs. disease stage. Figure 2. Spatial distribution of MRI predictors. Standardized elastic net coefficients for residual NPI-Q severity showed distributed effects across frontal, cingulate, parietal, and ventricular regions. Warm colors represent positive coefficients; cool colors represent negative coefficients. - MRI outperformed disease-stage prediction. - Prediction remained after stage, age, and sex adjustment. - Disease stage alone captured limited symptom-severity variation. - MRI predictors were distributed across brain regions.	- NPS severity varies within AD/MCI stages. - Structural MRI captures symptom-relevant brain variation beyond diagnosis. - NPS burden may reflect distributed brain-state differences. - MRI biomarkers may improve characterization of symptom heterogeneity. CONTACT For any questions regarding this poster, please contact Nam Hoang Le at le.h@wustl.edu Funding agency: The authors thank National Institutes of Health (NIH) K01AG083230 for their support in this research. 