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BACKGROUND

AI-based approaches have demonstrated the ability to reliably detect atrophy patterns from MRI data, achieving diagnostic accuracy comparable to expert neuroradiologists¹, and have shown sensitivity to subtle brain alterations in subjective cognitive decline (SCD)². However, SCD is heterogeneous and difficult to operationalize³, and MRI-based models often rely on large feature sets that can limit feasibility and interpretability in clinical practice. We developed an optimized model using machine learning approaches based on structural MRI measures **to cross-sectionally classify** cognitively unimpaired (CU), SCD, single-domain mild cognitive impairment (sd-MCI), and multi-domain mild cognitive impairment (md-MCI) **at risk of belonging to the AD continuum**.

METHODS

We studied 259 participants (98 CU, 69 SCD, 46 sd-MCI, and 46 md-MCI) from the Compostela Aging Study (CompAS⁴) and used 153 baseline structural MRI measures. We compared three single algorithms (Support Vector Machine [SVM], Random Forest [RF], and Logistic Regression [LR]) and a Soft-Voting Ensemble, evaluating performance using ROC curve analysis and reporting class-wise AUC under leave-group-out cross-validation. Prioritizing early stages and to favor a more optimized model, we selected **SVM** and reduced the feature set to **21 features** using performance-based selection and a collinearity-reduction procedure. Feature importance was assessed using permutation importance analysis.

RESULTS

The final structural MRI-based SVM model (21 features) showed **modest discrimination across** groups, with **class-wise AUC values of 0.66 (CU), 0.52 (SCD), 0.62 (MCIs), and 0.59 (MCIm)** (Figure 1). The greatest performance decreases under permutation were observed for right superior frontal volume (.049), right parahippocampal cortical thickness (.046), and right rostral anterior cingulate cortical thickness (.039), highlighting **frontal, medial temporal, and cingulate regions as the most influential** neuroanatomical features in differentiating the groups at risk of belonging to the AD continuum (Figure 2).

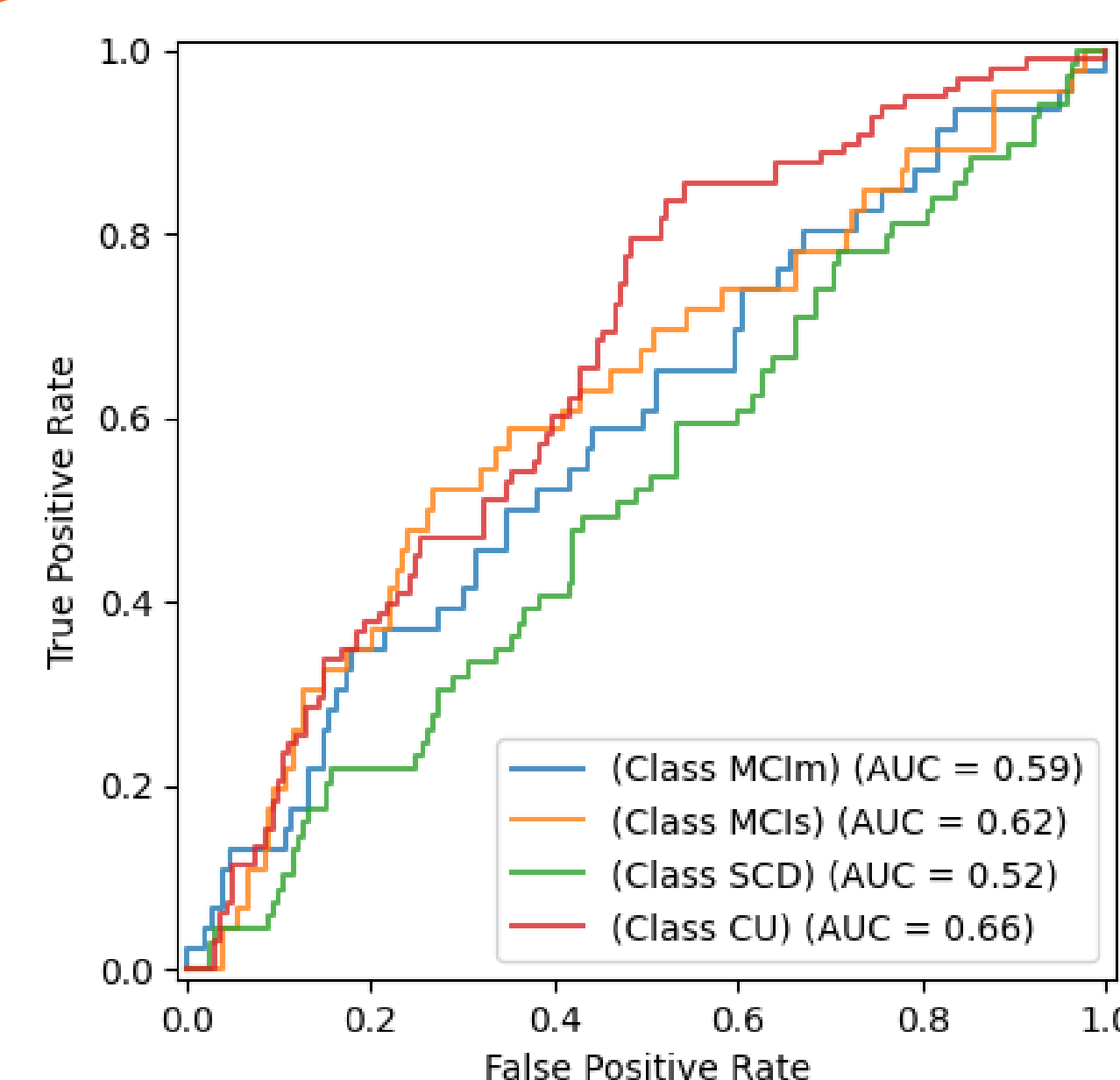


Figure 1. ROC curves for the structural MRI-based SVM model (21 features), with class-wise AUC values.

Note: AUC= Area Under the Curve; MCIm= Multi-domain MCI; MCIs= Single-domain MCI; SCD= Subjective Cognitive Decline; CU= Cognitively Unimpaired.

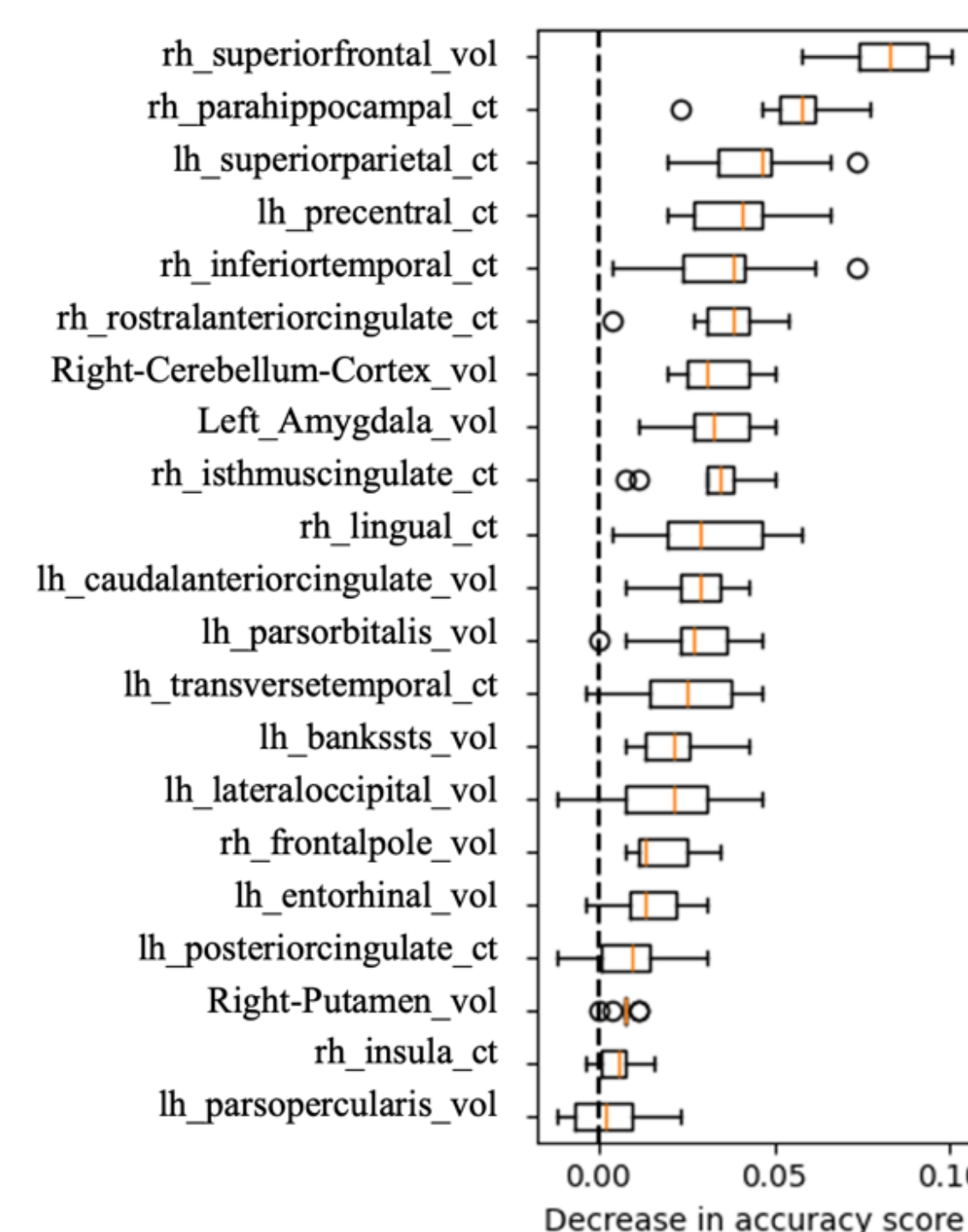


Figure 2. Permutation importance of the 21 features included in the structural MRI-based SVM model

Note: rh= right hemisphere; lh= left hemisphere; vol= volume; ct= cortical thickness.

CONCLUSIONS

The structural MRI-based SVM model achieved promising but modest classification performance, with frontal, medial temporal, and cingulate regions as key contributions. This supports the biological relevance of these areas but indicates that structural MRI alone may be insufficient given the heterogeneity subjacent to the diagnostic classification, particularly for SCD.



TAKE-HOME MESSAGE

- ✓ Structural MRI-based model with 21 features showed modest discrimination in differentiating CU, SCD and MCI subgroups.
- ✓ SCD was the most difficult group to classify using MRI alone.
- ✓ Frontal, medial temporal and cingulate regions emerged as the most influential neuroanatomical features.
- ✓ Additional longitudinal analyses should be performed to confirm the predictive capacity of MRI variables and potential synergies with multimodal measures that improve dementia prediction.

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