A comparison of machine learning based-composite cognitive test scores to track cognitive decline in early stages of Alzheimer's disease dementia: ADOPIC study

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INTRODUCTION

- Clinical trials of early dementia use cognitive measures that assess multiple cognitive domains to reflect disease progression
- Using precise cognitive measures for early Alzheimer's disease (AD) dementia progression is essential
- Current cognitive endpoints are computed by averaging standardized change from baseline scores (i.e., Preclinical Alzheimer Cognitive Composite (PACC)).

AIM

- Enhancing the detection of cognitive decline in Alzheimer's Disease Using machine learning-optimized cognitive composite scores
- Comparison of preclinical Alzheimer cognitive composite (PACC) against machine learning (ML)-optimized composite scores

METHODS

- Utilization of a large, harmonized dataset, Alzheimer's Dementia Onset and Progression in International Cohorts (ADOPIC) including ADNI, AIBL and OASIS datasets
- Construction of composite scores utilising ML-based algorithms: Uniform Manifold Approximation and Projection (UMAP), Principal Component Analysis (PCA), and Latent Variable Analyses (LVA)
- Clinical stratification: stable cognitively unimpaired (CU), CU progressing to mild cognitive impairment (MCI) or dementia, stable MCI, MCI progressing to dementia, and AD dementia
- Participants cognitive performance was investigated over 5 years before clinical progression and 5 years before the last visit for stables
- Implementation of linear mixed model (LMM) analysis to assess the validity of ML-based composites
- Computation of signal-to-noise ratios (SNRs) for each composite

RESULTS

Each ML-based cognitive composite showed sensitivity to cognitive decline in the progressor groups (Figure 1).

For the MCI progressors, PCA and UMAP composites had significantly higher SNRs than PACC ($P<0.01$; Figure 2), however, LVA performance was not significantly better than PACC. For the CU progressor group, SNRs for PCA and LVA did not show significant differences with PACC and UMAP performed significantly worse than PACC ($P<0.01$). However, PCA presented more generalised results compared to PACC in CU progressors.

CONCLUSION

The ML-based cognitive composite score computed using principal component analysis (PCA) improved the performance of tracking cognitive decline in MCI progressors compared to the PACC, while being comparable in CU progressors.

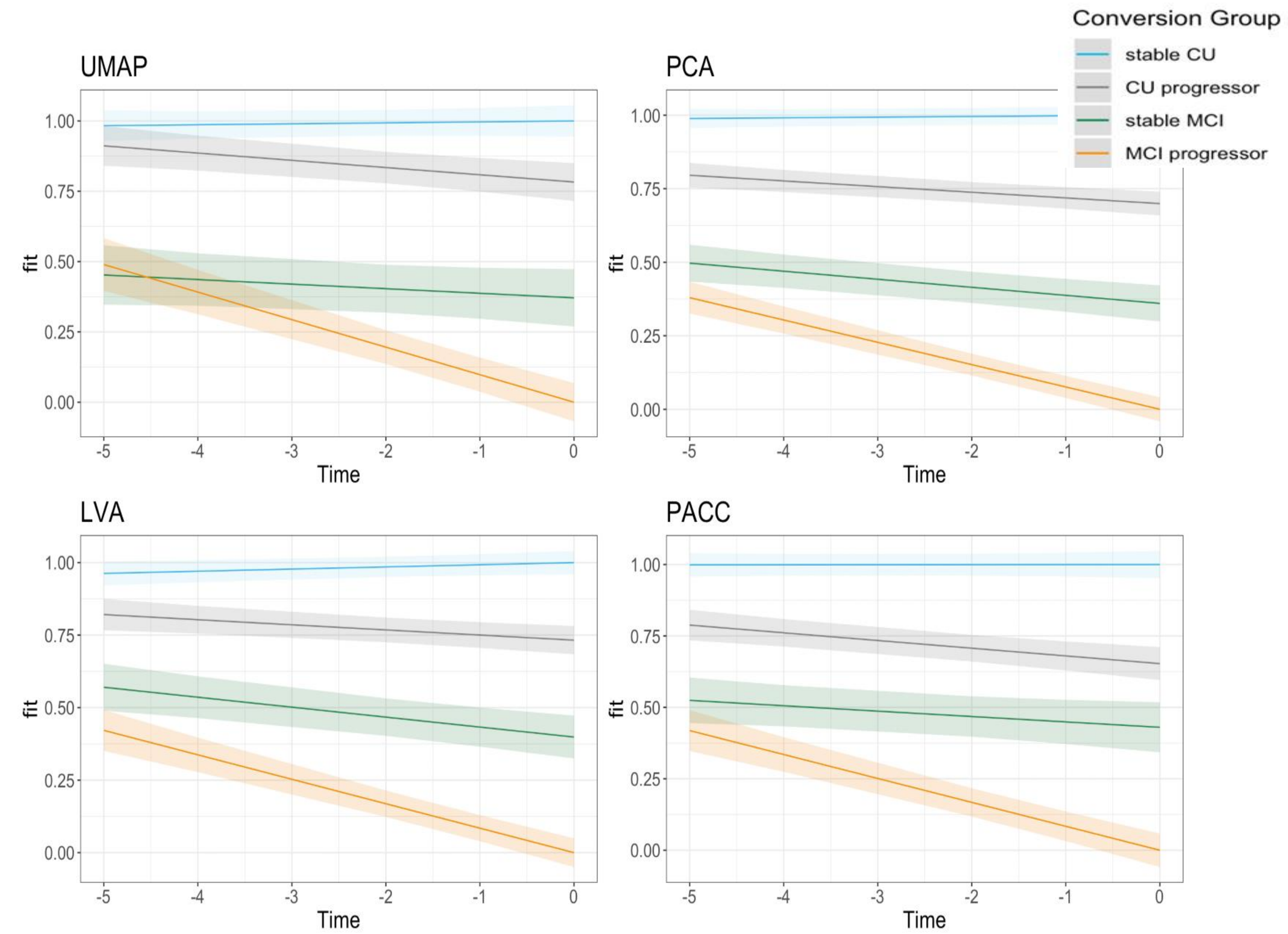

Figure 1. Comparison between UMAP, PCA, Latent variable analyses, and PACC scores based on LMM adjusting for age, stratified per clinical group.

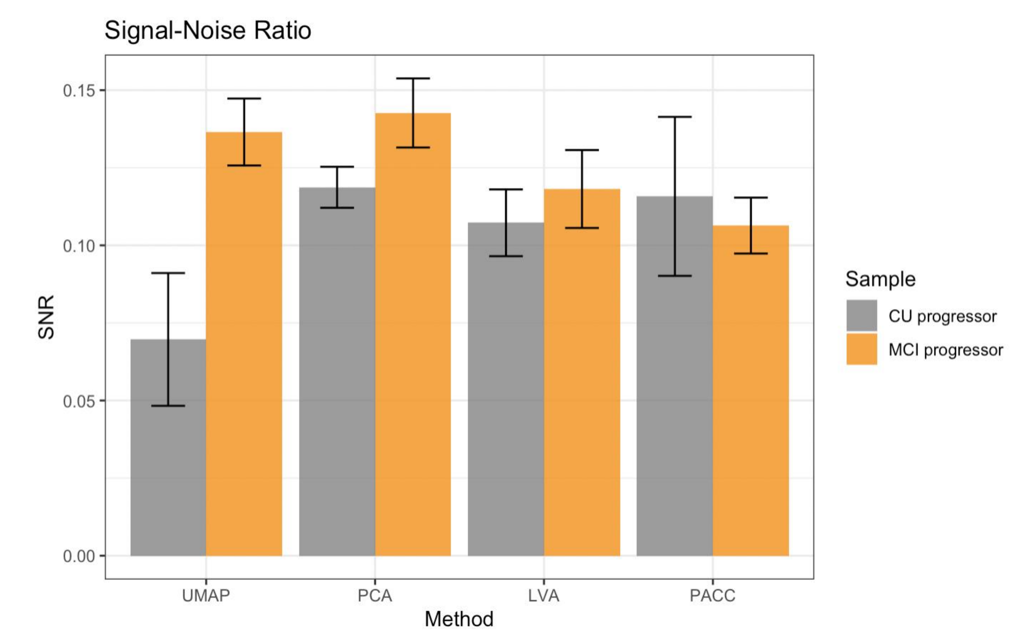

Figure 2: The differences in cognitive decline detected over time in CU progressors compared to those who remained cognitively unimpaired (in grey) and MCI progressors compared to those who stayed MCI over 5 years (in orange). The error bars indicate the mean SNRs over 4-fold cross validation splits. Higher mean SNRs show greater change (relative to stable group) detected by the composite score, corrected for variability. Smaller black error indicates better generality of the model.

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