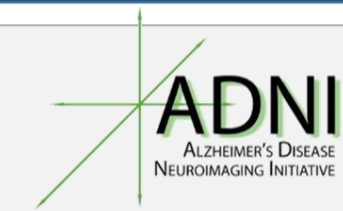


Background

- Static amyloid PET imaging requires the establishment of a suitable reference region (RR) for count normalization to compute standard uptake value ratios (SUVRs)
- The cerebellum has been used as a RRs for [F18]-AV45 amyloid imaging, but its sensitivity to capture longitudinal change in SUVR is debated [1]

Can we find a new RR for [F18]-AV45 amyloid PET imaging, which is more sensitive to capture longitudinal change than current RRs?

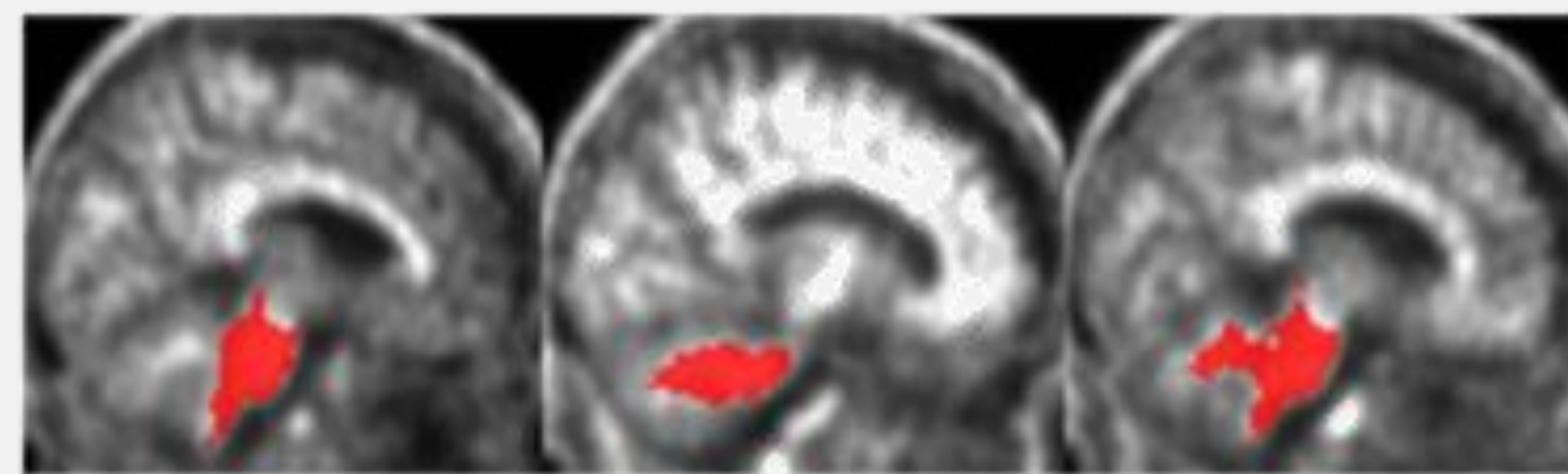
Methods



Detection & Validation Analysis

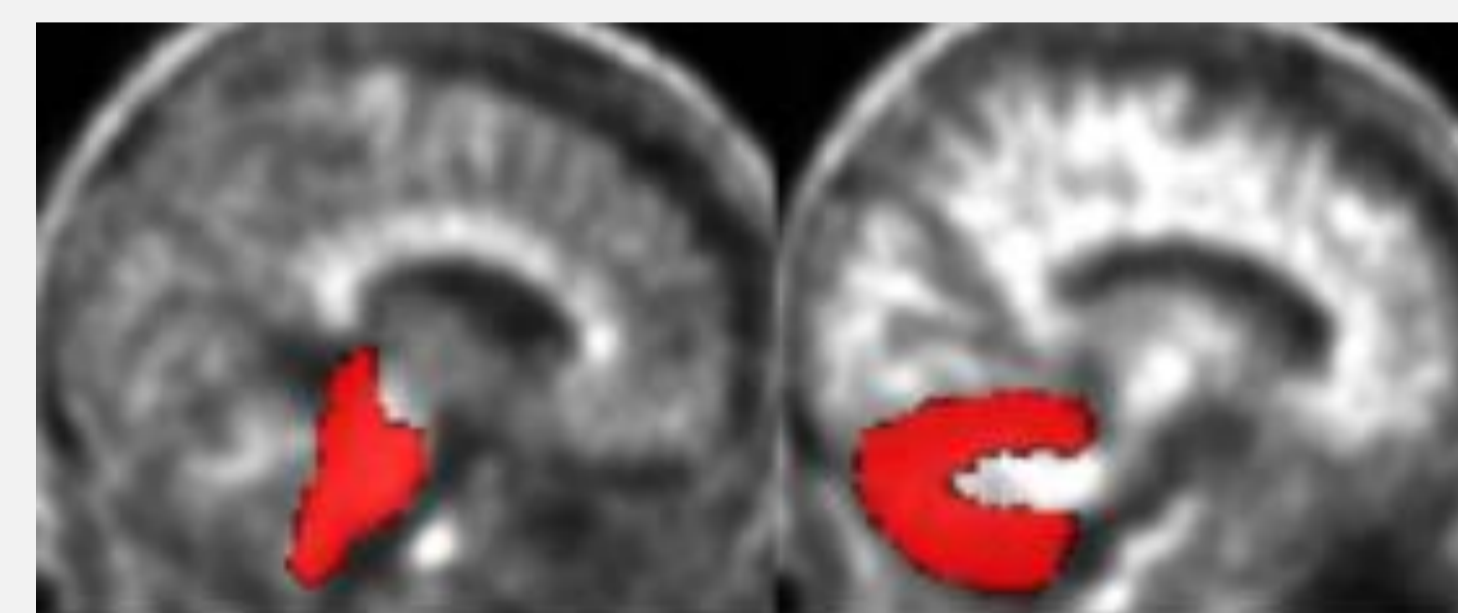
- [F18]-AV45 PET at BL
- 282 participants (135 CN- & 147 AD+)
- Mean age 73.0 (SD=7.5)
- Voxel-wise whole brain comparison (CN > AD)
- ROC analysis with mean global SUVR as a function of RR in an independent dataset

New RRs: CN > AD

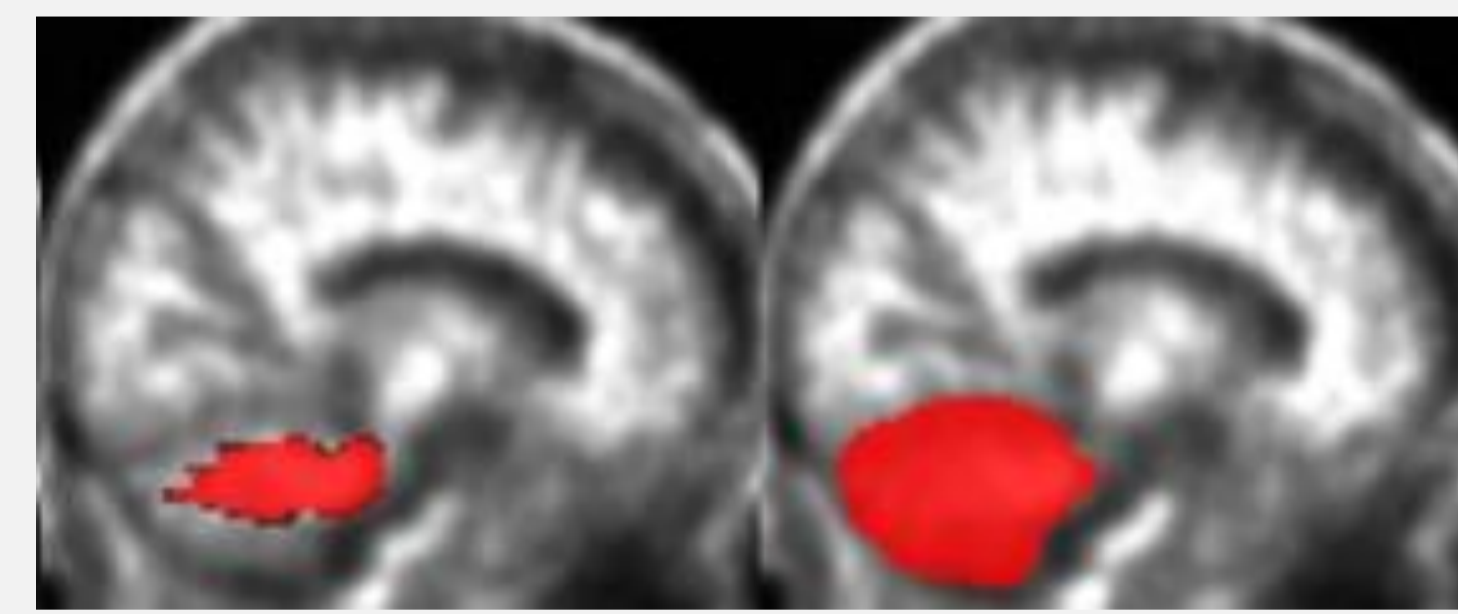


Brainstem Cerebellar white Composite

Commonly used RRs:



Brainstem Cerebellar grey



Cerebellar white Whole cerebellum

Longitudinal Analysis

- [F18]-AV45 PET at BL & FU
- 80 participants (19 CN+, 35 MCI+, 26 AD+)
- Mean age = 74.5 (SD=7.6)
- Follow-up timeframe = 2 yrs
- ROC analysis of SUVR change scores
- Pairwise comparisons of RRs

Tracer-specificity Analysis

- [F18]-FBB PET at BL
- 121 participants (47 CN+, 48 MCI+, 26 AD+)
- Mean age = 72.4 (SD=6.9)
- ROC analysis with mean global SUVR as a function of RR
- Pairwise comparisons of RRs

Correlation Analysis

- [F18]-AV45 PET at BL
- 80 participants (19 CN+, 35 MCI+, 26 AD+)
- Mean age = 74.5 (SD=7.6)
- Partial Pearson correlations between 2yrs cognitive change & mean global SUVR
- Covariates: age, sex, education, APOE4, group

Amyloid-positivity threshold: SUVR > 1.1

Results

All RRs showed poor longitudinal sensitivity in differentiating Aβ-positive groups from each other

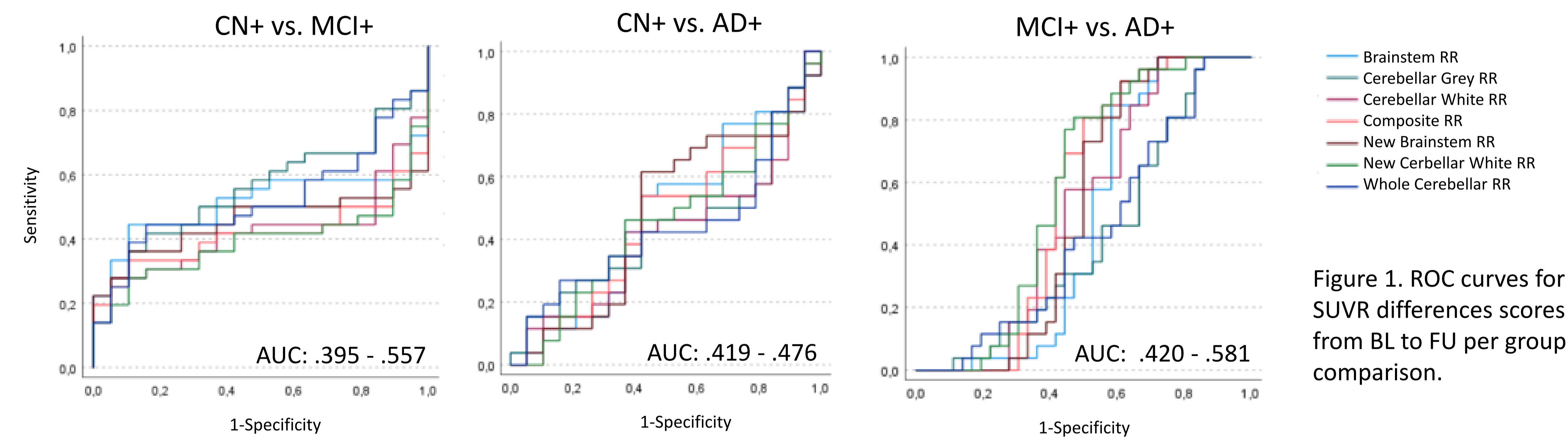


Figure 1. ROC curves for SUVR differences scores from BL to FU per group comparison.

All RRs can differentiate CN+ from AD+ but not CN+ from MCI+ when FBB scans are used

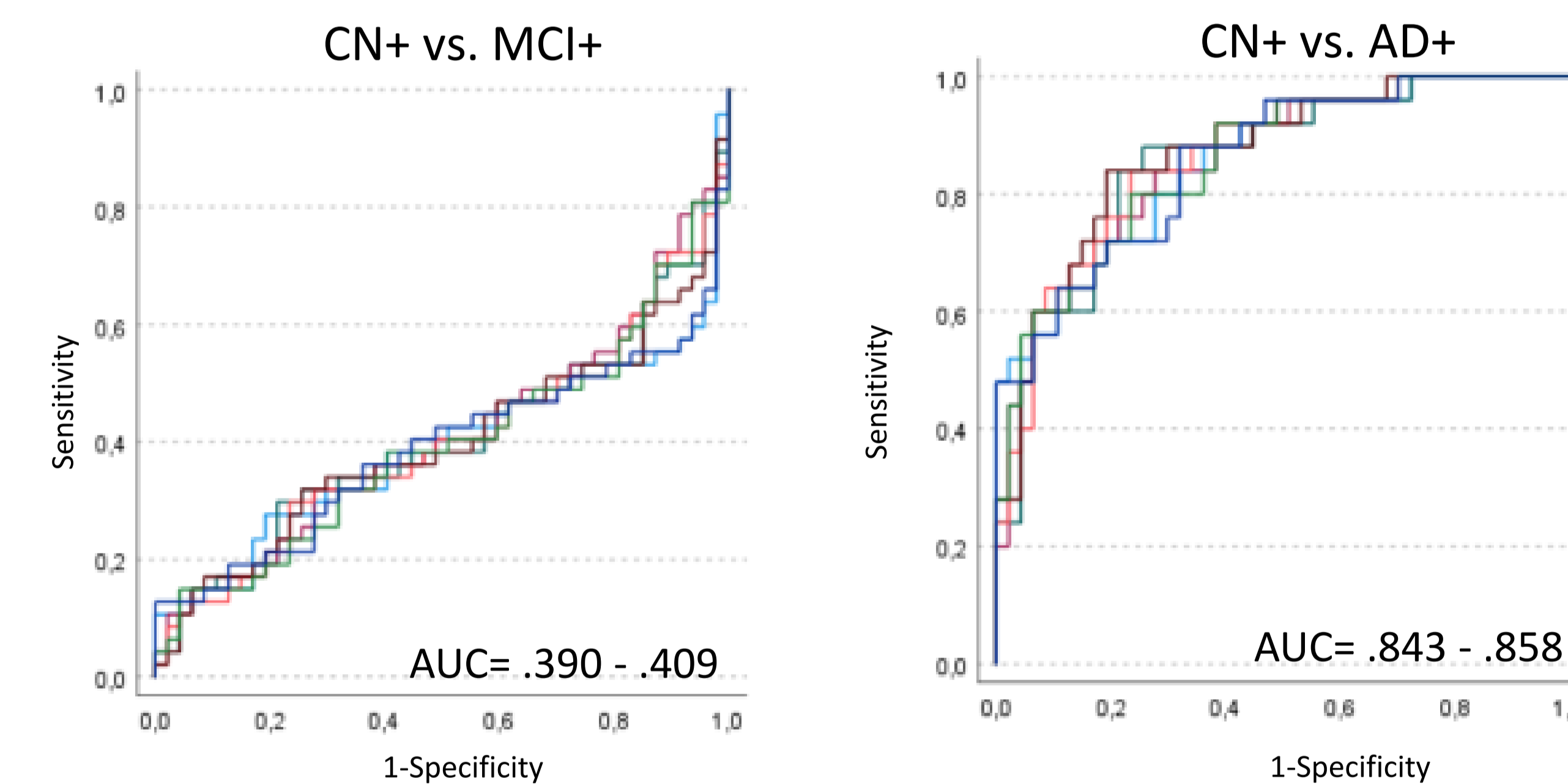


Figure 2. ROC curves for new and common RRs show high AUCs when differentiating CN+ from AD+ and low AUCs when differentiating CN+ from MCI+

New RRs show correlation with 2-year change in cognition

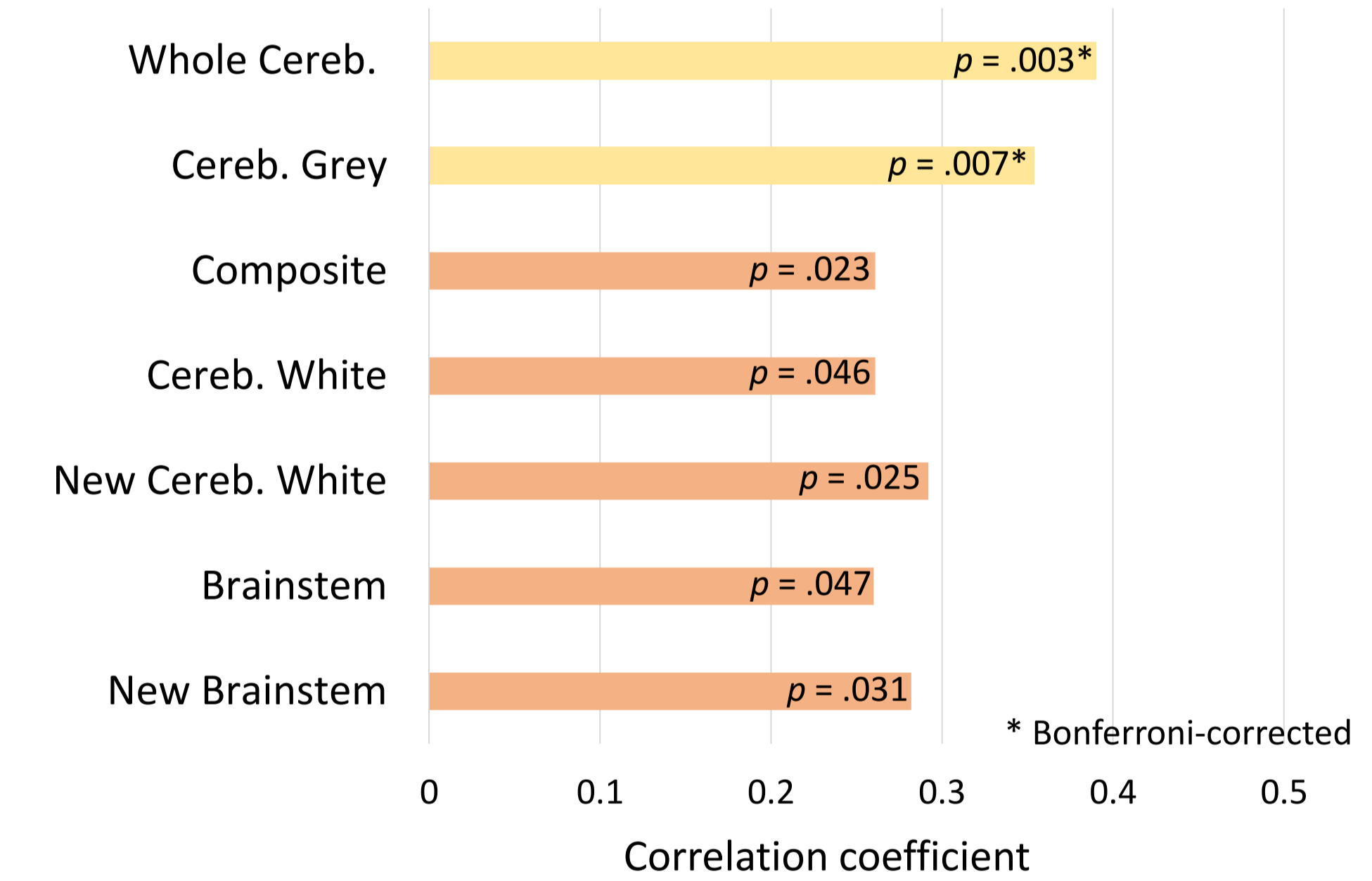


Table 1. Correlation coefficient between RR and cognition. Yellow = ADAS11; Orange = ADNI-executive functions

Conclusions

- All investigated RRs showed poor sensitivity in differentiating amyloid-positive groups based on longitudinal change in SUVR, indicating less differential changes in SUVR in amyloid positive individuals in 2 years
- Cross-sectionally all RRs, independent of amyloid-tracer, performed well dissociating CN+ from AD+, but significant variations were observed in differentiating CN+ from MCI+, indicating that different RRs should be used for different group comparisons
- Cognitive decline in executive function, but not memory, was captured with amyloid SUVR for most of the investigated RRs, suggesting that executive function decline may be more sensitive to capture advancing disease trajectories