SPARE-AD Scores from UPENN/SBIA: MRI-based biomarker of AD and MCI

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Summary

The SPARE-AD score (*Spatial Pattern of Abnormalities for Recognition of Early AD* (1)) is an imaging biomarker providing individualized scores of diagnostic and predictive value well beyond standard measures, such as hippocampal volumes. It was calculated for each individual, using an SVM based classifier with a linear kernel. Positive SPARE-AD values indicate the presence of an AD-like spatial pattern of brain atrophy in an individual, and negative values indicate normal brain structure. Baseline SPARE-AD scores have been found to be predictive of subsequent cognitive decline in MCI individuals (2) and to differentiate between MCI converters and non-converters (3) **on an individual patient basis**. The rate of longitudinal change of SPARE-AD was also found in (1) to be a good predictor of conversion from cognitively normal to AD. SPARE-AD scores are therefore likely to be good imaging biomarkers of early AD. Previous set of SPARE-AD scores that were uploaded to the LONI website were calculated from voxel-wise tissue density maps (RAVENS (4)). This new set of SPARE-AD scores are calculated using ROI-based volumetric image features as input, derived using a novel state-of-the-art multi-atlas segmentation method (5). This work was supported by R01AG14961 (PI: Christos Davatzikos, Ph.D.). Please contact Christos Davatzikos (Christos.Davatzikos@uphs.upenn.edu) for details. Pertinent software is available under https://www.cbica.upenn.edu/sbia/software/.

Method

ADNI subjects

Data from participants in the ADNI study [www.adni-info.org] were used. All baseline images available for download on ADNI's website [adni.loni.ucla.edu] in pre-processed forms (GradWarp, B1 Correction, N3, Scaled) by December 2014 were included in the analysis. The cohort included 230 cognitively normal (CN) individuals, 200 Alzheimer's (AD) patients, and 410 patients with Mild cognitive impairment (MCI).

Image preprocessing

The brain extraction from the downloaded images was achieved using a multi-atlas based method MASS (6). This was followed by a hierarchical parcellation using a multi-atlas based ROI segmentation method MUSE (5) (see Figure 1 below). Volumes extracted from these ROIs were then used for subsequent pattern analysis. These volumes are also available on the ADNI website [adni.loni.ucla.edu] for download.

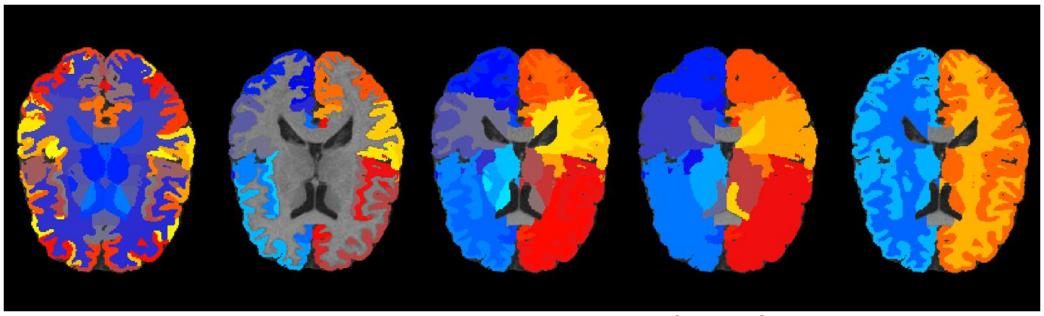

Figure 1: A sample hierarchical parcellation from MUSE

Pattern Analysis and the SPARE-AD score

Spatial patterns of tissue atrophy were evaluated via a SVM based classifer that separates the AD and CN participants with a hyper-plane in a high-dimensional space. These patterns of atrophy are learned from a training set and applied to a test set, in order to ensure that the model is derived from data other than the ones being evaluated. This was achieved by leave-one-out cross-validation, i.e. by leaving one subject out for testing, and using the remaining data for learning the most distinctive patterns, then applying the classifier to the left out subject.

Figure 2 and Table 1 shows the performance of the leave-one-out classification with an accuracy of 0.8977.

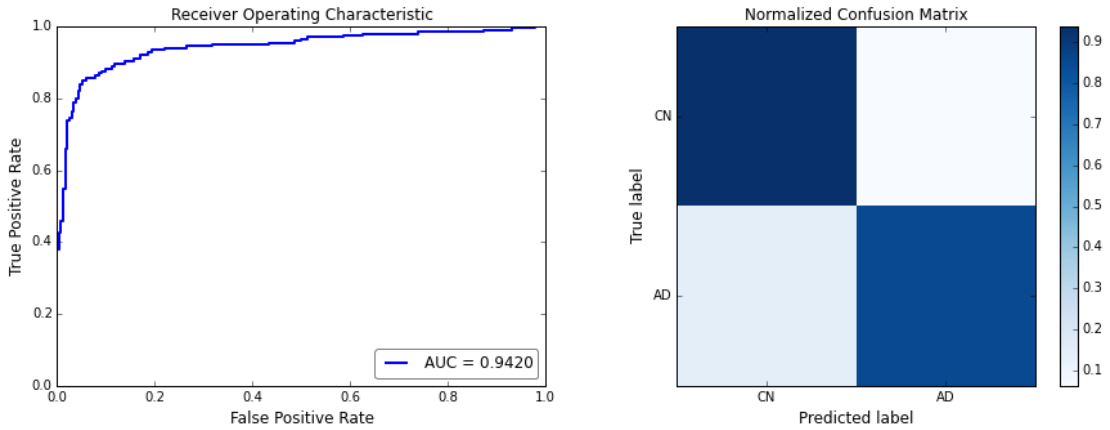

Figure 2: The ROC curve of the classification in AD/CN and the associated confusion matrix of predictions

The SPARE-AD scores for MCI subjects were obtained by training a model using the entire AD and CN dataset and then applying it to each one of the MCI scans. Figure 3 below shows the distribution of the SPARE-AD scores with respect to diagnosis (AD, MCI or CN) and with respect to MCI converters and non-converters.

METRIC	
Count	430
Accuracy	0.8977
AUC	0.9420
Sensitivity	0.85
Specificity	0.9391
True Positives	170
False Positives	14
True Negatives	216
False Negatives	30
Positive Predictive Value	0.9239
Negative Predictive Value	0.8780
False Positive Rate	0.0609
False Negative Rate	0.1500
False Discovery Rate	0.0761

Table 1: Classification metrics for the leave-one-out comparison between AD and CN subjects

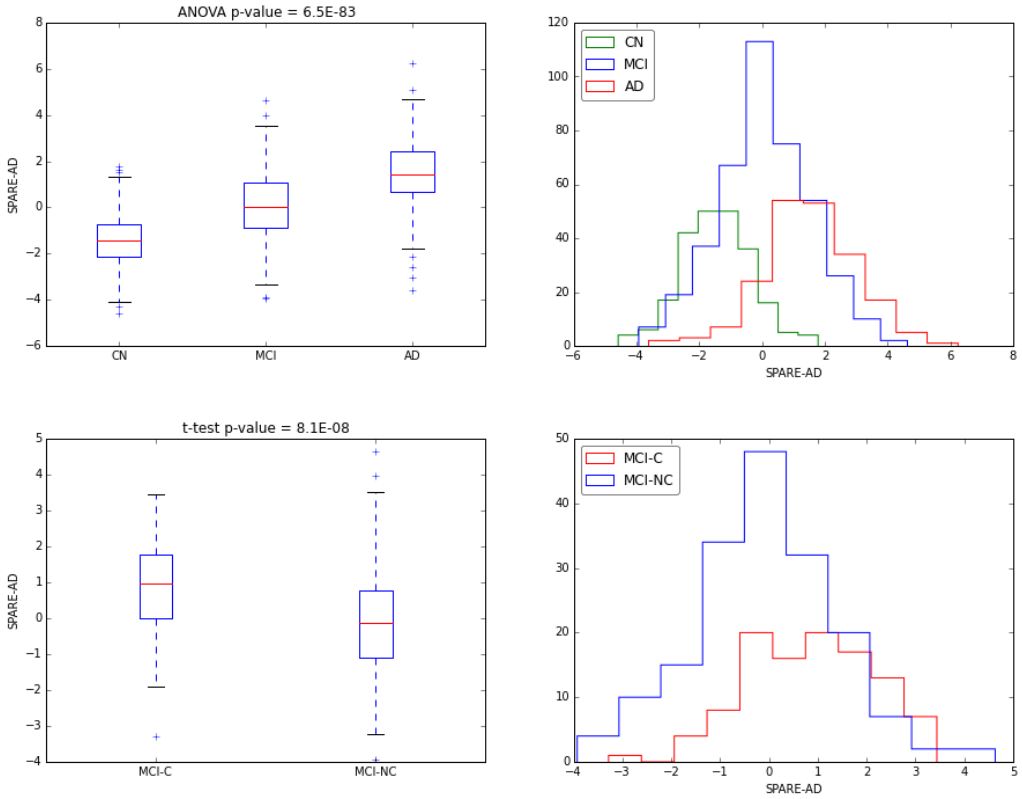

Figure 3: Distribution of the SPARE-AD scores among the CN, MCI and AD subjects (top) and among the MCI converters and non-converters (bottom)

Dataset Name	Date Submitted
SPARE-AD UPENN	July 21, 2016

ADNI Alzheimer's Disease Neuroimaging Initiative

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