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

Jimit Doshi, Guray Erus and Christos Davatzikos
Section of Biomedical Image Analysis, Center for Biomedical Image Computing and Analytics, Department of Radiology, University of Pennsylvania

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. The SPARE-MCI score is an extension of SPARE-AD, in that it was built from MCI individuals who converted to AD within 18 months and MCI individuals who remained stable for over 36 months. SPARE-MCI is therefore likely to be a better MRI biomarker of MCI to AD conversion. 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 410 patients with Mild cognitive impairment (MCI), out of which 103 subjects converted to AD within 18 months (MCI-SC) and 227 subjects remained stable for over 36 months (MCI-LS).

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.

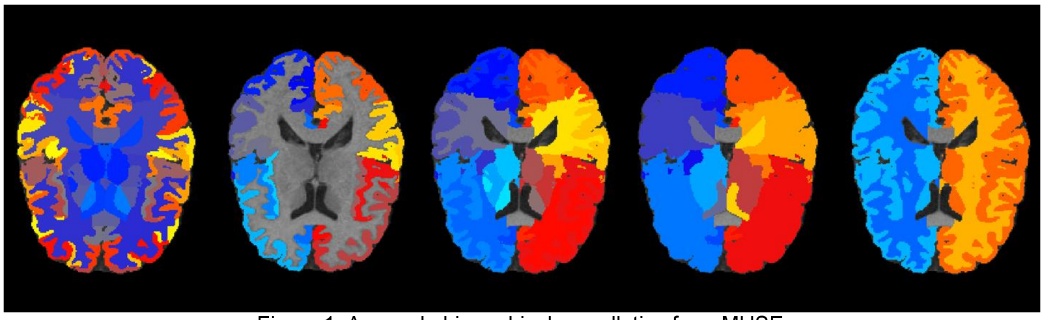

Figure 1: A sample hierarchical parcellation from MUSE

Pattern Analysis and the SPARE-MCI score

Spatial patterns of tissue atrophy were evaluated via a SVM based classifer that separates the MCI-SC and MCI-LS 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. To account for the imbalance in the sample sizes, a weighted SVM classifier was used in the construction of the training model, using class weights that were inversely proportional to class frequencies in the training data.

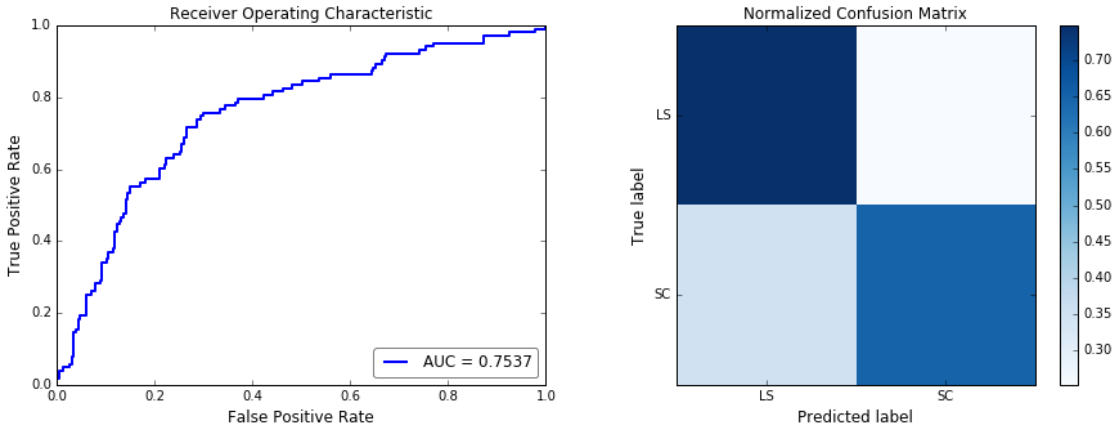

Figure 2: The ROC curve of the classification in MCI-SC/MCI-LS and the associated confusion matrix of predictions

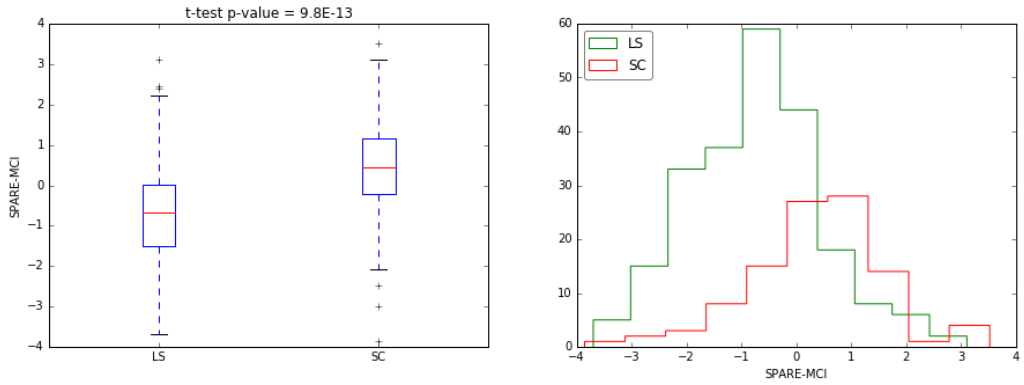

Figure 3: Distribution of the SPARE-MCI scores among the MCI-SC and MCI-LS subjects

METRIC	
Count	330
Accuracy	0.7182
AUC	0.7537
Sensitivity	0.6505
Specificity	0.7489
True Positives	67
False Positives	57
True Negatives	170
False Negatives	36
Positive Predictive Value	0.5403
Negative Predictive Value	0.8252
False Positive Rate	0.2511
False Negative Rate	0.3495
False Discovery Rate	0.4597

Table 1: Classification metrics for the leave-one-out comparison between MCI-SC and MCI-LS subjects

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

Bibliography

1. *Longitudinal progression of Alzheimer's-like patterns of atrophy in normal older adults: the SPARE-AD index.* **Christos Davatzikos, Feng Xu, Yang An, Yong Fan, Susan M. Resnick.** 2009, Brain, pp. 2026-2035.
2. *Spatial patterns of brain atrophy in MCI patients, identified via high-dimensional pattern classification, predict subsequent cognitive decline.* **Yong Fan, Nematollah Batmanghelich, Chris M. Clark, Christos Davatzikos.** 4, 2008, NeuroImage, Vol. 39, pp. 1731–1743.
3. *Baseline and longitudinal patterns of brain atrophy in MCI patients, and their use in prediction of short-term conversion to AD: Results from ADNI.* **Chandan Misra, Yong Fan, Christos Davatzikos.** 4, 2009, NeuroImage, Vol. 44, pp. 1415–1422.
4. *Voxel-based morphometry using the RAVENS maps: methods and validation using simulated longitudinal atrophy.* **Davatzikos, Christos, Ahmet Genc, Dongrong Xu, Susan M. Resnick.** 6, 2001, NeuroImage, Vol. 14, pp. 1361-1369.
5. *MUSE: MUlti-atlas region Segmentation utilizing Ensembles of registration algorithms and parameters, and locally optimal atlas selection.* **Jimit Doshi, Guray Erus, Yangming Ou, Susan M. Resnick, Ruben C. Gur, Raquel E. Gur, Theodore D. Satterthwaite, Susan Furth, Christos Davatzikos.** 15, 2016, NeuroImage, Vol. 127, pp. 186–195.
6. *Multi-Atlas Skull-Stripping .* **Jimit Doshi, Guray Erus, Yangming Ou, Bilwaj Gaonkar, Christos Davatzikos.** 12, 2013, Academic Radiology, Vol. 20, pp. 1566–1576.
7. *Voxel-based morphometry using the RAVENS maps: methods and validation using simulated longitudinal atrophy.* **Davatzikos, Christos, Ahmet Genc, Dongrong Xu, Susan M. Resnick.** 6, 2001, NeuroImage, Vol. 14, pp. 1361-1369.

Notice: This document is presented by the author(s) as a service to ADNI data users. However, users should be aware that no formal review process has vetted this document and that ADNI cannot guarantee the accuracy or utility of this document.