SUB-CORTICAL SHAPE MORPHOLOGY AND VOXEL-BASED FEATURES FOR ALZHEIMER’S DISEASE CLASSIFICATION

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Introduction

Alzheimer’s disease (AD) is the most general cause of degenerative dementia. Our work presents an unsupervised framework for the classification of Alzheimer’s disease (AD) patients into diagnostic groups: AD, EMCI (Early Mild Cognitive Impairment), LMCI (Late Mild Cognitive Impairment) and Normal Control (NC), based on features extracted from select sub-cortical region-of-interests (ROIs).

We use a combination of features, namely:
- Gray-matter voxel-based intensity variations
- Structural alterations (shape), extracted with a spherical harmonics framework
- By combining multi-modality features, this work demonstrates the potential of exploiting complementary features to improve cognitive assessment

Dataset

- 600 T1-weighted subject MRI scans (variable resolution, volumetric 3D MPRAGE or equivalent protocols)
- 4 separate cohorts: AD, EMCI, LMCI and NC. Criteria: age, cognitive symptoms, neuropsychological test score like Mini-Mental State Examination (MMSE), Clinical Dementia Rating (CDR) and Memory Box score

ADNI: Alzheimer’s Disease Neuroimaging Initiative
- Launched in 2003 as a $60 million 5-year public private partnership

Methodology and Pipeline

1. ROBEX[1] Brain Extraction: Fits a triangular mesh, constrained by a shape model, to the probabilistic output of a supervised brain boundary classifier
2. Atlas-based sub-cortical segmentation
   - Registration: FLIRT toolkit, part of the FMRIB Surface Library (FSL) package
   - Transformation Matrix: Subject space to MN152 atlas space. Affine transformation, correlation ratio similarity measure and trilinear interpolation
   - Inverse Transformation Matrix: AAL[2] atlas space to subject space; Nearest neighbour interpolation
3. Morphology Feature Extraction (SPHARM PDM)
   - Sub-cortical masks, including the hippocampus, as inputs
   - SPHARM representation: 3D surface mesh decomposed using the spherical harmonics basis function
   - SPHARM PDM[3]: SPHARM representation transformed into a triangulated surface, containing 1002 landmark coordinates
   - Features: x, y and z coordinates of the SPHARM-PDM landmark coordinates
4. Classification Models
   - Combined feature vector: voxel-intensities and shape features
   - Principal component analysis (PCA) transformation for dimensionality reduction
   - Supervised classification: Two-class SVM, both linear and RBF kernels

Results

Classification accuracy (ACC), sensitivity (SEN), and specificity (SPE/SV) values using methods I, II, and III, for 6 different pairs of binary diagnostic groups obtained from the ADNI database. † stands for p < 0.001

Conclusion:
- Shape analysis coupled with mean VIs gives superior results as compared to only shape coordinates or only voxel intensities indicating that these features provide complementary information
- Results show linear SVM is slightly superior than (or equal to) RBF SVM
- Our approach performs particularly well for the more challenging classification problems: NC vs EMCI (75.5%), AD vs LMCI (76.8%) and EMCI vs LMCI (71%)
- Future work will involve combining additional bio-markers such as cortical thickness data, volume, voxel-wise tissue probability and density of gray matter.

Acknowledgements
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References

Extracted sub-cortical structures from 12 ROIs obtained from the atlas-based segmentation approach

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<th>AD</th>
<th>EMCI</th>
<th>LMCI</th>
<th>NC</th>
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<td>Mean Age (Min, Max)</td>
<td>75.73 (56,92)</td>
<td>74.29 (56,92)</td>
<td>72.84 (56,90)</td>
<td>76.27 (49,94)</td>
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<td>Gender (M/F)</td>
<td>57/42</td>
<td>94/70</td>
<td>101/88</td>
<td>119/85+ (undeline)</td>
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<td>Number of subjects</td>
<td>99</td>
<td>164</td>
<td>167</td>
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Participant Distribution