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

POLYTECHNIQUE MONTRÉAL

Shashank Tripathi*, Seyed Hossein Nozadi*, Mahsa Shakeri*† and Samuel Kadoury*†

for the Alzheimer's Disease Neuroimaging Initiative

** MedICAL Laboratory, Polytechnique Montreal, Canada*

† CHU Sainte-Justine Research Center, Montreal, Canada

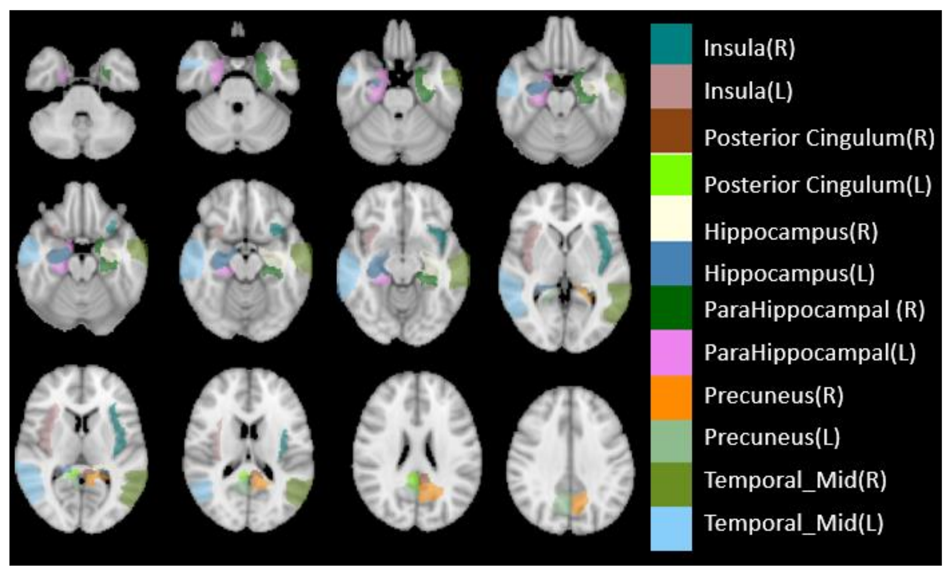
Introduction

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**



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

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, neuropsycological test score like Mini-Mental State Examination (MMSE), Clinical Dementia Rating (CDR) and Memory Box score

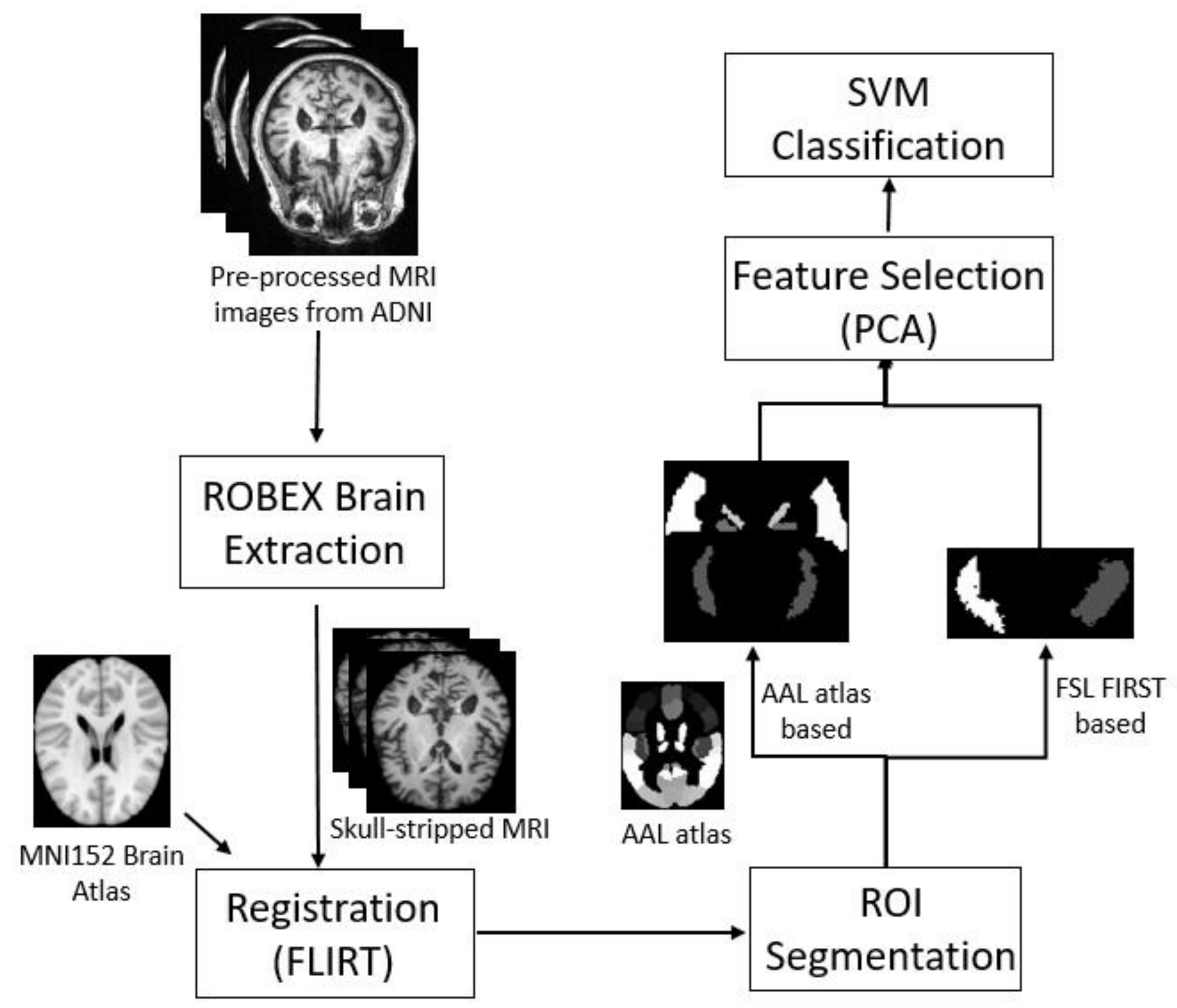
ADNI: Alzheimer's Disease Neuroimaging Initiative

- Launched in 2003 as a $60 million 5-year public private partnership

	AD	EMCI	LMCI	NC
Mean Age (Min, Max)	75.73 (56,92)	74.29 (56,92)	72.84 (56,90)	76.27 (49,94)
Gender (M/F)	57/42	94/70	101/88	119/88+1 (undefined)
Number of subjects	99	164	167	170

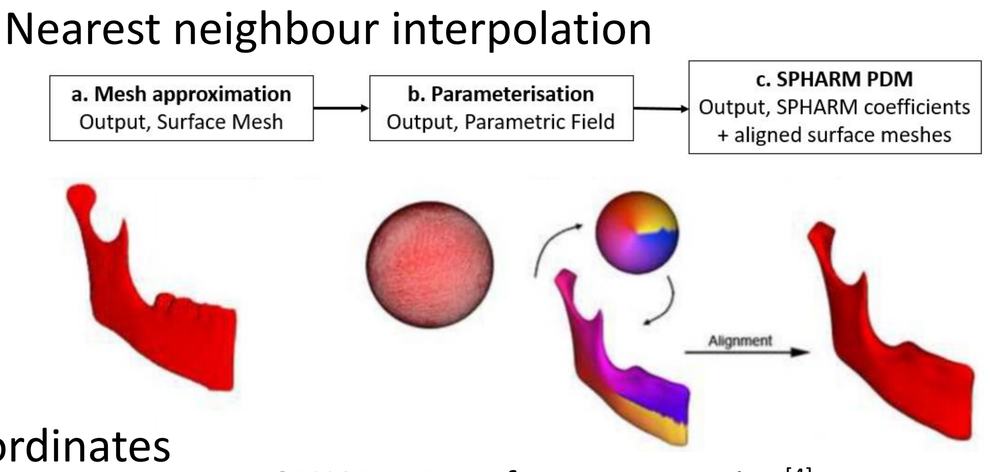
Participant Distribution

Methodology and Pipeline



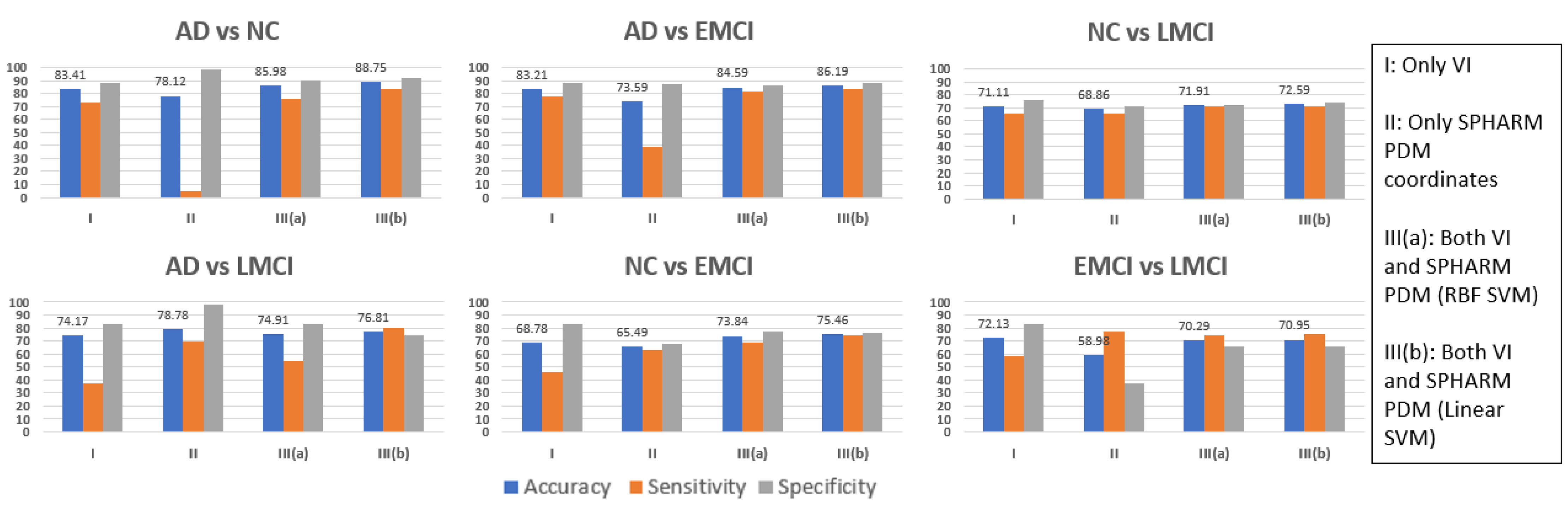
Overview of the proposed pipeline for classification of AD patients using a multi-region (n=12) approach combining intensity and shape-based features

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 MNI152 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



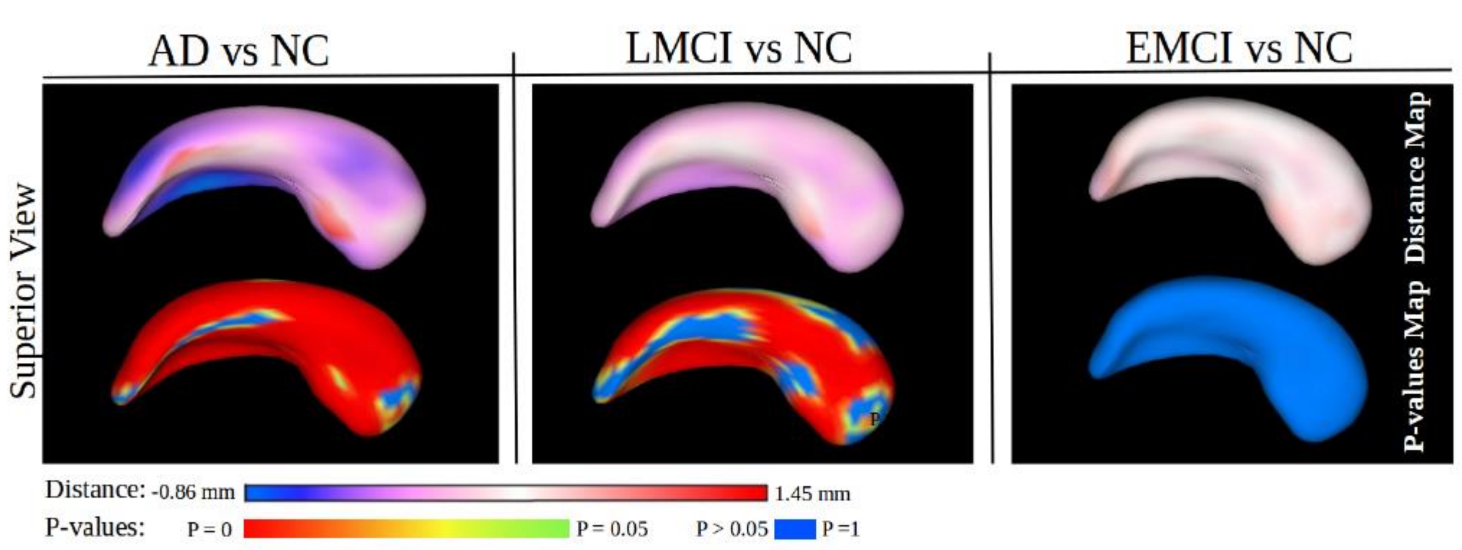
SPHARM PDM feature extraction[4]

Results



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

- For testing the statistical significance of performance measures, unpaired student t-tests were performed between the methods (I), (II) and (III)
- The accuracy values are directly proportional to the morphological separation in disease progression



Morphological group differences between AD, LMCI, EMCI groups with normal controls (NC). Distance and p-value maps are shown for each pair of cognitive groups

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

Data collection and sharing for this project was funded by the Alzheimer's Disease Neuroimaging Initiative(ADNI). The project was funded by Canadian Institutes of Health Research.

References

[1] Iglesias et al, "Robust brain extraction across datasets and comparison with publicly available methods", IEEE transaction on medical imaging, vol 30 p: 1617-1634; [2] Tzourio-Mazoyer et al, "Automated Anatomical Labelling of Activations in SPM", NeuroImage 2002, 15: 273-289 [3] Gerig et al "Shape analysis of brain ventricles using SPHARM", MMBIA 2001, pp 171-178 [4] Image source: Cevidanes et al, "3D Quantification of Mandibular Asymmetry" Oral Surg Oral Med Oral Pathol Oral Radiol, Endod (2011), 111(6), 757-770

ADNI Alzheimer's Disease Neuroimaging Initiative

CIHR IRSC