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Background

Alzheimer's disease (AD) is the most common form of dementia, which is a progressive brain disorder mostly occurring in the middle or late life.

- A decline in memory and other cognitive functions.
- A lethal disease.
- AD has become a global burden with 26.6 million patients
- By 2046, 1.2% of the global population will be affected by AD.

Many machine learning methods have been proposed to aid the diagnosis of AD based on high dimensional features extracted from various neuroimaging biomarkers. The early diagnosis of AD can be naturally modelled to be a **multi-class classification problem**:

- AD: Patients of Alzheimer's Disease
- MCI: Mild Cognitive Impairment, a prodromal stage of AD, which can be further categorized into convertor or non-convertor depending on whether the subject transfer to AD in 3 years
- NC: Normal Control, people without AD syndromes

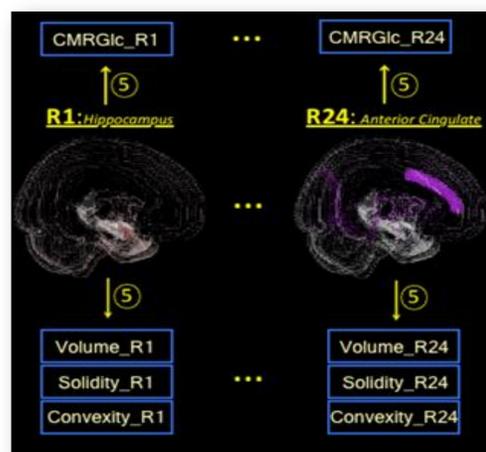
Contribution

We proposed an automated diagnosis framework based on deep learning architectures. Comparing to the previous workflows, our framework:

- significantly boosts the classification performance
- capable of multi-class classification
- reduce the reliance on prior knowledge
- semi-supervised learning
- easy to examine the features

Dataset & Feature Extraction

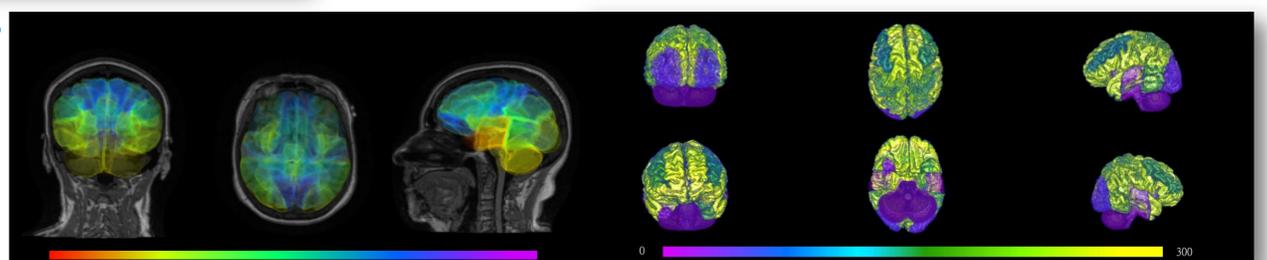
All the neuroimaging data obtained from ANDI database were registered to the ICBM_152 template using Image Registration Toolkit (IRTK). Numerical anatomical measurements (volume, shape, curvature, etc.) are extracted from neuroimaging data (MRI and PET) accompanied with CSF measurements.



Visualization of Extracted Features

We also proposed a method to visualize the brain features learnt from deep learning architecture. We mapped the stability score

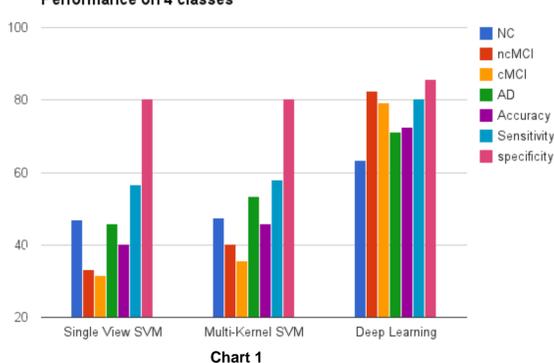
$$S_j = \sum_m \frac{\sum_j D_j^{(m)}}{D_j^{(m)}}$$



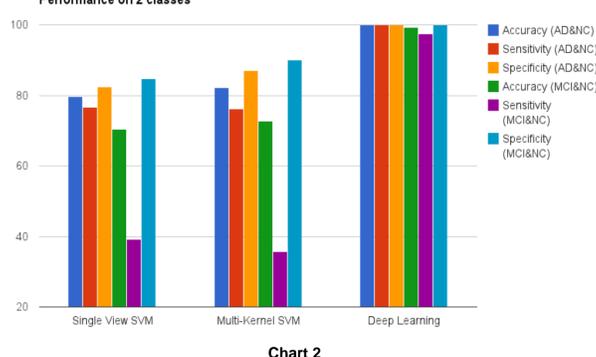
Visualization of the sensitivity of AD progression of each brain region of interest

Experimental Results & Conclusion

Performance on 4 classes



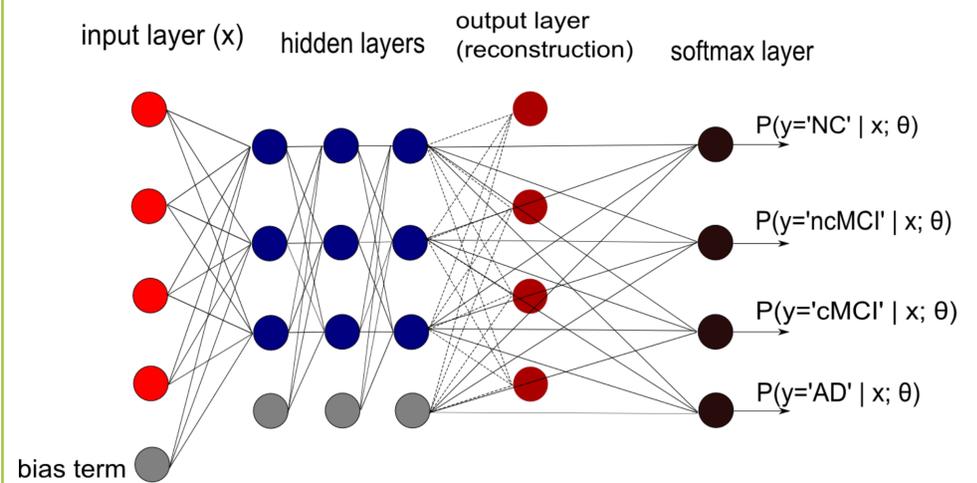
Performance on 2 classes



Our proposed framework outperformed the widely used single-kernel / multi-kernel Support Vector Machine (SVM) in both two-class and four-class classification tasks, as shown in Chart 1 and Chart 2, respectively.

The deep learning architecture was proven to demonstrate a significant gain in the performance of AD diagnosis. This study may also have a great potential to lead to a new perspective for computer-aided-diagnosis in other biomedical fields.

Training Methodology



Representation Learning with Stacked Autoencoders

The feature representation can benefit from the depth of the learning structure, which learns more profound representations from the manifolds extracted by the previous hidden layers.

To train this unsupervised model, we applied the representation loss as the objective function for optimization, e.g.

$$L(W, b, x, z) = \min_{W, b} E(W, b, x, z) + \gamma \|W\|_2^2 + \beta K(W, b, x),$$

where $K(W, b, x) = \sum_j^n ID_{KL} \left(\rho \parallel \frac{1}{m} \sum_{i=1}^m h_j(x^{(i)}; W, b) \right)$. The parameters can be optimized by gradient descent based algorithms, such as L-BFGS.

Classification with Softmax Regression

We push a softmax output layer on the top of the trained autoencoder stack containing only previous hidden layers. The softmax layer uses a different activation function, which might have nonlinearity, different from the one applied in previous layers. The softmax activation function can be derived as

$$h_i^l = \frac{e^{w_i^l h^{l-1} + b_i^l}}{\sum_j e^{w_j^l h^{l-1} + b_j^l}}$$

where h_i^l can be used as an estimator of $P(Y = i | x)$, where Y is the associated label of input data vector x . Similar to the training procedure of Deep Belief Network, we can further fine-tune all the parameters in the network with respect to the classification criterion.