Alzheimer's Disease Classification using Volumetric and Cortical Thickness Features with Deep Learning and Linear Discriminant Analysis

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Abstract. We used volumetric and cortical thickness features to predict the class of Alzheimer's disease dementia as Alzheimer's disease,mild cognitive impairment, or healthy control. We present a deep learning based computational model pipeline for feature extraction using multiple stacked auto-encoders from structural magnetic resonance imaging. A second model is presented for Alzheimer's disease classification using linear discriminant analysis on the same extracted feature set. Our models are trained using a publicly available database and tested on the CAD-Dementia challenge dataset, where the true data labels are unknown to the authors.

1 Introduction

Alzheimer's disease is a lethal neuro-degenerative disease that results in memory loss and impairs both verbal and non-verbal skills such as holding conversations and recognizing friends and families. Physicians classify the progression of Alzheimer's disease as Alzheimer disease (AD) or mild cognitive impairment (MCI) based on the Clinical Dementia Rating scale [1], mini-mental state examination [2], and logical memory examinations [2]. MCI is the prodromal stage of AD where minor problems with thinking and language may be observed, while AD subjects are unable to function independently and need assistance from others. In this work, we use volumetric and cortical thickness derived features to classify subjects as AD, MCI, or healthy control (HC) for a group of clinical cases in the CADDementia Grand challenge [4]. Decreases in the size of brain regions are important biomarkers of Alzheimer's disease[7]. Cortical thinning is known to be a reliable biomarker of Alzheimer's disease [8]. We propose volumetric and cortical features in the classification of Alzheimer's disease using 1) Deep Learning and 2) Linear Discriminant Analysis.

2 Data

The proposed models are trained on subjects selected from the initial screenings of the "complete annual year 2 visits" downloaded from Alzheimer's Disease Neuroimaging Initiative (ADNI) [5]. The training data is of magnetic field strength

1.5T [5]. Sørensen et al., the top performing team in the 2014 CADDementia Challenge, demonstrated that the "complete annual year 2 visit" dataset was successful in training their model for the competition [6].The class distribution for the subjects for the selected dataset is 171 HC, 232 MCI, and 101 AD. The test dataset consists of 3T structural MRI of unknown class labels. We submitted the classification labels for the test set to CADDementia challenge organizers and they would report the accuracy on the test data. The CADDementia organizers have not released the test subject labels, thus this challenge remains an opportunity for researchers to validate their Alzheimer's disease classification models. The CADDementia organizers also provided a 30-subject training dataset with labels for teams to use prior to submission to CADDementia. We use this 30-subject dataset for testing our model.

3 Methodology

The proposed pipeline consists of the following steps: preprocessing, feature, feature extraction and classification.

3.1 Preprocessing

The Freesurfer suite v5.3 is used for preprocessing [9]. We performed the cortical reconstruction process with the additional hippocampus subfields flag. Subject test_emc_039 was assigned class AD because Freesurfer pipeline was unable to produce cortical measurements for this subject and its visual appearance of atrophy.

3.2 Features

The Freesurfer tool is used to extract a total of 119 features which consist of 57 volumetric features and 62 cortical features. The volumetric features are measured in mm^3 and were normalized to the brain size using the total intracranial volume measurement from the Freesurfer. Most regions of interest consist of left and right volumetric measurements, which were used as independent features. The cortical thickness features were normalized within their respective datasets so that their values ranged between zero and one. Cortical thickness features included measurements from both sides of the brain for a total of 62 features.

3.3 Deep Learning

We implemented a 5-layer Stacked Auto-encoder (SAE) with an input layer, three hidden layers, and an output layer. The SAE have been used on volumetric features to predict the labels for AD and MCI [11]. We expanded the SAE in the DeepLearnToolbox [10] from one hidden layer to three hidden layers. An outline of the 3-layer SAE is shown in Fig. 1.

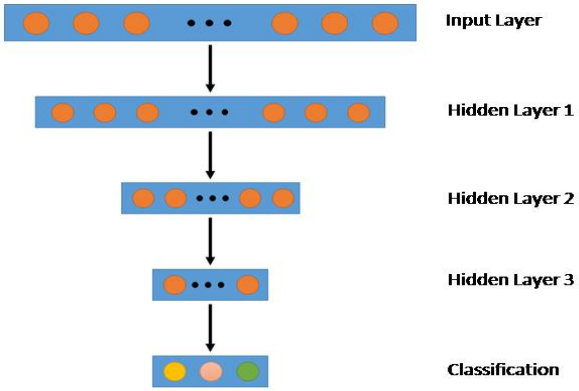

Fig. 1. The Deep Learning Network used for Alzheimer's disease classification.

The SAE is a popular variant of Deep Neural Network that combines several auto-encoders. Let x be an input vector of size m and n be the number of hidden neurons. The compressed representation of input x can be written as,

$$h = f(W^1 x + b^1), \tag{1}$$

where h denotes the compressed representation of the input, W^1 denotes the input to hidden weight vector (also known as encoder weights) of size m by n, b^1 represents the bias and f represents a non-linear activation function (in this study we consider sigmoid). The input is then reconstructed by utilizing another decoding weight matrix W^2 of size n by m. This reconstructed input is considered as the final output of the auto-encoder. The error function of the auto-encoder can be written as,

$$E = \frac{1}{2}||x - f(W^2 h + b^2)||_2^2, \tag{2}$$

where b^2 represents the bias. We minimized this error using the regular back propagation method with gradient descent. he first hidden layer was trained using the aforementioned 119 features. A greedy layer-wise training was used to train the hidden layers [12]. After the pre-training, the auto encoders are stacked together with the pre-trained weights to design the final deep network. A classifier layer is incorporated at the end to perform the classification of AD, MCI, and HC. We also applied dropout for both pre-training and fine-tuning the network.

3.4 LDA

For the 3-class training dataset, LDA yields two significant Eigen vectors that yield the target separation among the classes. The training dataset is projected

on to these two Eigen vectors to obtain the discriminating feature space. A polynomial kernel is used for the SVM classifier to train and test the data folds in a 10-fold cross validation. The resultant Eigen vectors from the training dataset are used to project the test datasets on the same subspace. The LDA projection for 3-class dataset reduces the train or test data from N-dimensional to a 2-dimensional feature space following a separation between each pair of classes. We project the CADdementia testing dataset with 30 subjects on the LDA subspace derived from the ADNI dataset. An SVM classifier with polynomial kernel is trained with the LDA projected features from the ADNI dataset and tested with the CADdementia dataset with 30 subjects.

3.5 Pipeline Processing Time

The majority of this work was completed on a dual-six core Xeon processor for 64 gigabytes of memory. The process time for computing is broken down as follows: Freesurfer pipeline 24 hours per subject, Matlab feature vector construction and normalization 15 minutes per data set, and 15 minutes to train the 3-layer SAE.

4 Preliminary Results

We present three classification metrics for the evaluation of our models prior to submission to CADDementia: training accuracy, 10-fold cross validation accuracy, and accuracy on the 30 labeled subjects that CADDementia provided. For the SAE, we achieved 70.3% training accuracy and 59.6% 10-fold cross validation accuracy on the training set. On the 30-subject CADDementia dataset, we achieved 66.7% accuracy. For LDA, a 10-fold cross validation is conducted on this projected training data using SVM which results in 69.8% accuracy. The CADdementia test accuracy is found to be 56.67%.

5 Discussion and Conclusion

We present two models for Alzheimer's disease classification using features derived from structural MRI. Cortical thickness and volumetric regions of interest are known biomarkers of the spatial atrophy patterns associated with Alzheimer's disease. We applied deep learning with multiple hidden layers to extract trends in the non-linear spatial atrophy patterns associated with Alzheimer's disease. Deep neural networks and LDA models using volumetric and cortical features have great potential in aiding a physician's assessment of Alzheimer's disease because it is noninvasive and rapidly provides an objective analysis.

Acknowledgments

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