A Novel Deep Learning based Multi-Class Classification Method for Alzheimer's Disease Detection using Brain MRI Data

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Abstract. Alzheimer's Disease is a severe neurological brain disorder. It destroys brain cells causing people to lose their memory, mental functions and ability to continue daily activities. Alzheimer's Disease is not curable, but earlier detection can help improve symptoms in a great deal. Machine learning techniques can vastly improve the process for accurate diagnosis of Alzheimer's Disease. In recent days deep learning techniques have achieved major success in medical image analysis. But relatively little investigation has been done to applying deep learning techniques for Alzheimer's Disease detection and classification. This paper presents a novel deep learning model for multi-Class Alzheimer's Disease detection and classification using Brain MRI Data. We design a very deep convolutional network and demonstrate the performance on the Open Access Series of Imaging Studies (OASIS) database.

Keywords: Alzheimer's Disease, Deep Learning, Convolutional Neural Network, MRI, Brain Imaging.

1 Introduction

Alzheimer's Disease affects people in a numerous way. Patients suffer from memory loss, confusion, difficulty in speaking, reading or writing. Eventually, they may forget about their life and could not recognize even their family members. They can forget how to perform daily activities such as brushing teeth or combing hair. As a result, it makes people anxious or aggressive or to wander away from home. Alzheimer's Disease can even cause death in elder people. There are three major stages in Alzheimer's Disease - very mild, mild and moderate. Detection of Alzheimer's Disease (AD) is still not accurate until the patient reaches a moderate AD. But early detection and classification of AD are critical for proper treatment and preventing brain tissue damage. Several things are needed for proper medical assessment of AD. Physical and neurobiological exams, Mini-Mental State Examination (MMSE), and patient's detailed history

are required for accurate AD detection and classification. In recent years, doctors are using brain Magnetic Resonance Imaging (MRI) data for earlier detection of Alzheimer's Disease.

Researchers have developed several computer-aided diagnostic systems for accurate disease detection. They have developed rule-based expert systems from the 1970s to 1990s and supervised models from 1990s [11]. The supervised systems are trained with feature vectors extracted from medical image data. Extracting the features needs human experts that often require a lot of time, money and effort. With the advancement of deep learning models, now we can extract features directly from the images without the engagement of human expert. So researchers are focusing on developing deep learning models for accurate disease detection and classification.

Deep learning models have been successfully applied for different medical image analysis such as MRI, Microscopy, CT, Ultrasound, X-ray, Mammography, etc. Deep models have shown a prominent result for organ and substructure segmentation, several disease detection and classification in areas of pathology, brain, lung, abdomen, cardiac, breast, bone, retina, etc. But there is little existing work for AD detection using deep learning models. From previous research in the medical domain, it has been proved that MRI data can perform a significant role for early detection of Alzheimer's Disease. For our research work, we plan to analyze brain MRI data using deep learning model for Alzheimer's Disease detection and classification.

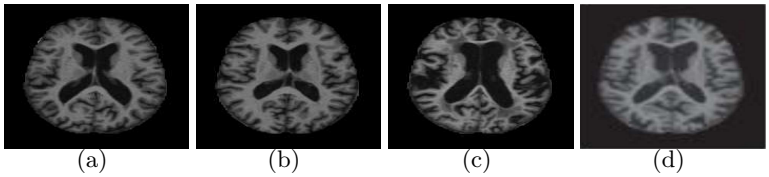

Fig. 1. Example of different brain MRI images presenting different AD stage. (a) Non-demented; (b) very mild dementia ; (c) mild dementia; (d) moderate dementia.

Machine learning studies using neuroimaging data for developing diagnostic tools helped a lot for automated brain MRI segmentation and classification. Most of them use handcrafted feature generation and extraction from the MRI data. After that, the features are fed into machine learning models such as Support Vector Machine, Logistic regression model, etc. These multi-step architectures are complex and highly dependent on human experts. Besides, the size of datasets for neuroimaging studies is small. While image classification datasets used for object detection and classification has millions of image (for example, ImageNet

database [18]), neuroimaging datasets typically have less than 1000 images. But to develop robust neural networks we need a lot of images. Because of the scarcity of large image database, it is important to develop models that can learn useful features from the small dataset. For our proposed system, we are using deep learning model which eliminates the need for hand-crafted feature generation. Deep learning models transform input to output and build a feature hierarchy from simple low-level features to complex high-level feature. The popular deep learning model used for image analysis is Convolutional Neural Network (CNN). We propose a very deep CNN model for analyzing the brain MRI images and classifying them into different AD stages.

Alzheimer's disease has a certain progressive pattern of brain tissue damage. It shrinks the hippocampus and cerebral cortex of the brain and enlarges the ventricles [19]. Hippocampus is the responsible part of the brain for episodic and spatial memory. It also works as a relay structure between our body and brain. While average reduction per year in the hippocampus is between 0.24 and 1.73 %, Alzheimer's disease patients suffer shrinkage between 2.2 and 5.9 % [1]. The reduction in hippocampus cause cell loss and damage specifically to synapses and neuron ends. So neurons can't communicate anymore via synapses. As a result, brain regions related to remembering (short term memory), thinking, planning, and judgment are affected [19]. The degenerated brain cells have low intensity in MRI images [5], [29]. Fig. 1 shows some brain MRI images presenting different AD stage.

Sometimes the signs that distinguish Alzheimer's disease MRI data can be found in normal healthy aged brain MRI data. Extensive knowledge and experience are required to distinguish the AD MRI data from the aged normal MRI data. A robust and effective automated machine learning model will help immensely the scientists and medical persons working for AD diagnosis and ultimately assist the timely treatment of the AD patients. A generic automated Alzheimer's Disease detection and classification framework is shown in Fig. 2. Our proposed deep CNN model can detect early stages of Alzheimer's disease and successfully classify the major three different stages. We have experimented the performance of the proposed model on the Open Access Series of Imaging Studies (OASIS) database [15] which provides T1-weighted MRI scans with demographics and clinical assessment data. Our main contributions are as follows:

- ☐ We propose a novel and faster framework for Alzheimer's disease detection analyzing brain MRI data.
- ☐ Our framework can classify three major stages of Alzheimer's disease.
- ☐ We demonstrate that utilizing hyper-parameters from a very deep image classifier CNN can help feature learning from small medical image dataset.

The rest of the paper is organized as follows: Section 2 presents briefly about the related work. Proposed Alzheimer's Disease detection and classification framework is presented in Section 3. Experimental details and results are

described in Section 4. Finally, we present future work and conclude the paper in section 5.

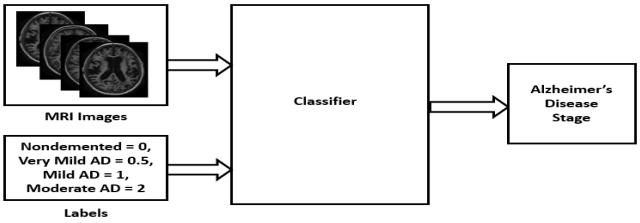

Fig. 2. Diagram of a generic Alzheimer's disease detection and classification framework.

2 Related Work

Developing an automated Alzheimer's Disease detection and classification model is a pretty challenging task. But there is some remarkable research work in this area. Dimensional reduction and variations methods were used by Aversen et al. [2] to analyze structural MRI data. They have used both SVM binary classifier and multi-class classifier to detect AD MRI images using Alzheimers Disease Neuroimaging Initiative (ADNI) database [9]. Brosch et al. [3] developed a deep belief network model and used manifold learning for AD detection from MRI images. Katherine Gray developed a multi-modal classification model using random forest classifier to detect AD from MRI and PET data [6]. Gupta et al. have developed a sparse autoencoder model for AD, Mild Cognitive Impairment (MCI) and healthy control (HC) classification using ADNI dataset [7]. Hosseini-As et al. adapted a 3D CNN model for AD diagnostics [8]. Kloppel et al. used linear SVM to detect AD patients using T1 weighted MRI scan [10]. Liu et al. [12] developed a deep learning model using a subset of ADNI dataset and classified AD and MCI patients. Liu et al. have developed a multimodal stacked auto-encoder network using zero-masking strategy. Their target was to prevent loss of any information of the image data. They have used SVM to classify the neuroimaging features obtained from MR/PET data [13].

Magnin et al. utilized an anatomically labeled brain template to identify regions of interest from whole brain images and concluded that it could be used for early AD detection [14]. Morra et al. compared several model's performances for AD detection including hierarchical AdaBoost, SVM with manual feature and SVM with automated feature [16]. Payan et al. [17] trained sparse autoencoders and 3D CNN model to classify AD, MCI and HC patients using ADNI dataset. Sarraf et al. used fMRI data and deep LeNet model on ADNI dataset for AD detection [20]. Suk et al. developed an autoencoder network based model for AD

detection. They have extracted features from magnetic current imaging (MCI) and MCI-converter structural MRI and PET data and performed classification using multi-kernel SVM. Several complex SVM kernels were used in their AD detection approaches [21], [22], [23], [24]. Vemuri et al. used SVM to develop three separate classifiers with MRI, demographic and genotype data to classify AD and healthy patients [28].

3 Proposed Network Architecture

In this section, the proposed Alzheimer's disease detection and classification framework would be presented. The proposed model is shown in Fig. 3. Our model is inspired by Inception-V4 network [25]. After the preprocessing is done, the input is passed through a stem layer. A stem layer includes several 3*3 convolution layers, 1*1 convolution layer, and max pooling layer. There is seven 3*3 convolution layer connected in different stages and two filter-expansion layers (1*1 convolution layer). Inception-A module has four filter-expansion layers, three 3*3 convolution layer, and one average pooling layer. Inception-B module has four filter-expansion layers, four 1*7 convolution layer, two 7*1 convolution layer and one average pooling layer. Inception-C module has four filter-expansion layers, three 1*3 convolution layer, three 3*1 convolution layer and one average pooling layer. Reduction-A module has one filter-expansion layer, three 3*3 convolution layer, and one 3*3 max-pooling layer. The Reduction-B module has two filter-expansion layers, two 3*3 convolution layer, one 1*7 convolution layer, one 7*1 convolution layer and one 3*3 max pooling layer. The input and output of all these modules pass through filter concatenation process. We have redesigned the final softmax layer for Alzheimer's disease detection and classification. The softmax layer has four different output class: nondemented, very mild, mild and moderate AD. The network takes an MRI image as input and extracts layer-wise feature representation from the first stem layer to the last drop-out layer. Based on this feature representation, the input MRI image is classified to any of the four output classes.

To measure the loss of the proposed network, we have used cross entropy. The Softmax layer takes the feature representation, f_i and interprets it to the output class. A probability score, p_i is also assigned for the output class. If we define the number of Alzheimer's disease stages as m, then we get

$$p_i = \frac{exp(f_i)}{\sum_i exp(f_i)}, i = 1, ..., m$$

and

$$L = -\sum_i t_i log(p_i),$$

where L is the loss of cross entropy of the network. Back propagation is used to calculate the gradients of the network. If the ground truth of an MRI image is

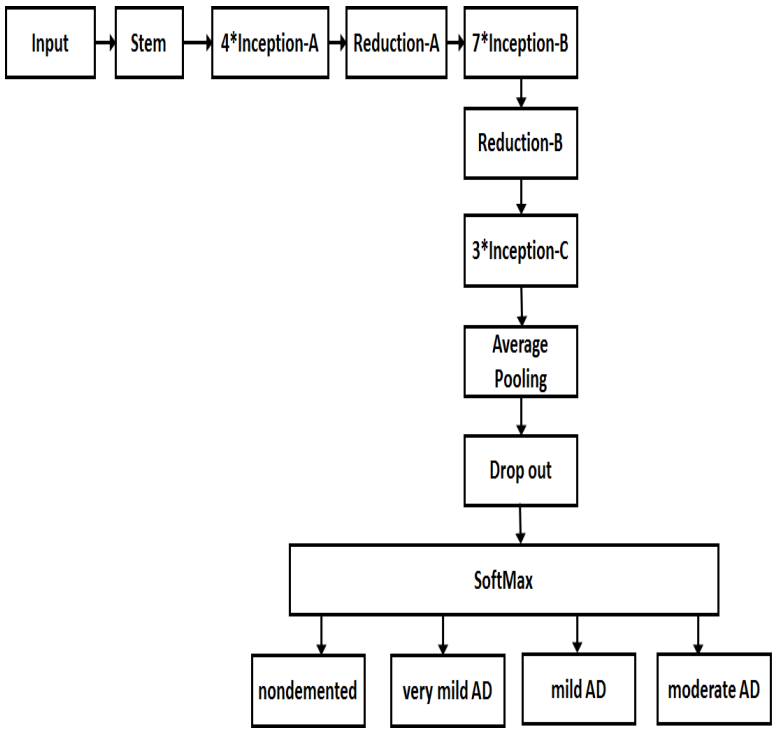

Fig. 3. Block diagram of proposed Alzheimer's disease detection and classification framework.

denoted as t_i, then,

$$\frac{\partial L}{\partial f_i} = p_i - t_i$$

There is numerous possible combination for the hyper-parameters of a network. It takes a lot of time and effort to decide a stable hyperparameter set for a network. To reduce this time, we have used hyperparameters of the Inception-V4 model [25] instead of random initialization. The weights and biases of the inception-v4 model [25] pre-trained with ImageNet database [4] provide our network an efficient hyperparameter set. As a result, the model has a sense of better feature detector and can use that knowledge for learning features from the small medical image dataset. We have trained our model with OASIS [15] dataset. To prevent overfitting in the network, we have applied data augmentation technique such as reflection and scaling.

4 Experiments

4.1 Dataset

OASIS dataset is prepared by Dr. Randy Buckner from the Howard Hughes Medical Institute (HHMI) at Harvard University, the Neuroinformatics Research Group (NRG) at Washington University School of Medicine, and the Biomedical Informatics Research Network (BIRN) [15]. There are 416 subjects aged 18 to 96, and for each of them, 3 or 4 T1-weighted MRI scans are available. 100 of the patients having age over 60 are included in the dataset with very mild to moderate AD. Fig. 4 shows some sample brain MRI images from OASIS dataset.

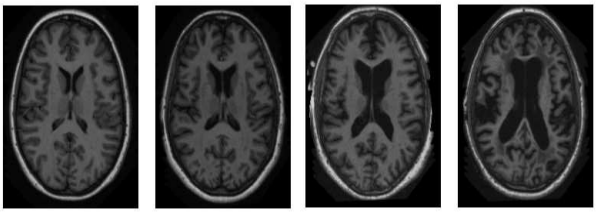

Fig. 4. Sample images from OASIS dataset.

4.2 Implementation Details

We have implemented the proposed deep CNN model for Alzheimer's disease detection and classification using Tensorflow [30] and Python on a Linux X86-64 machine with AMD A8 CPU, 16 GB RAM and NVIDIA GeForce GTX 770. We have applied data augmentations techniques - scaling and reflection on the images. Since the dataset is small, 5-fold cross validation is performed on the dataset. For each fold, We have used 70% as training data, 10% as validation data and 20% as test data. The input size of the Inception-V4 network [25] is 299*299*3. To fit the MRI data, we have designed the input size of our network as 299*299*1. We have modified the Inception B and C module so that they can accept the MRI data. The convolutional filter size of Inception-B is 1154 in the original network. We made it to 1152 to fit the MRI data. The convolutional filter size of Inception-C is 2048 in the original network. We made it to 2144 to fit the MRI data. The network is optimized with the RMSProp [27] algorithm and early-stopping is used for regularization. The decay of the network is 0.9 and batch size is 8. The base learning rate is set to 0.045.

4.3 Results

To our best knowledge, our approach is the first one for Alzheimer's disease detection and classification using deep learning method on OASIS dataset. So, we are not comparing it with previous traditional methods. The current accuracy of our method is 73.75%. The confusion matrix is presented in Table 1. The proposed model is much faster and takes less than 1 hour to train and test the OASIS dataset for Alzheimer's disease detection and classification. This performance is superior than all previous traditional methods. It would take weeks for human experts to analyze and classify all the MRI data. We do not need any manual hand-crafting for feature generation in our model.

We have implemented another deep model with traditional inception module and 22 layers following GoogleNet [26] architecture and compared the performance with our proposed model. The performance comparison is presented in Table 2.

Table 1. CONFUSION MATRIX

AD stage	Nondemented	Very mild	Mild	Moderate
Nondemented	52	0	0	0
Very mild	2	4	0	0
Mild	7	0	8	0
Moderate	3	0	1	3

Table 2. FIVE-FOLD CROSS VALIDATION PERFORMANCE ACCURACY COMPARISON ON THE OASIS DATASET

No. of epochs	Traditional Inception Network	Proposed Model
5	60.00%	71.25%
10	64.25%	73.75%

5 Conclusion

An automated Alzheimer's disease detection and classification framework is crucial for the early detection and treatment of the AD patients. We have proposed a deep CNN model for automated Alzheimer's disease detection and classification. We have demonstrated the performance of the model on OASIS dataset. Our method is faster, and it does not need any handcrafted feature, and it can handle the small medical image dataset. We have provided an one step analysis for the brain MRI data for AD detection and classification. There are several improvements possible for the proposed approach. In future, we hope to work

with other MRI AD dataset such as ADNI and achieve similar or better performance. We want to apply transfer learning and check if it produces better result than the proposed approach. Currently, we are working with different hidden layers and convolutional filters to do more optimization to find a more efficient model to get better results. Finally, we want to explore semi-supervised and unsupervised deep learning methods for multi-class Alzheimer's disease detection and classification.

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