

International Journal of Engineering Sciences & Research Technology

(A Peer Reviewed Online Journal)

Impact Factor: 5.164



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ABSTRACT

Alzheimer's disease(AD),the world's most common form of dementia, is one of the worst thing that can ever happen to a person during his lifetime. With a poorly understood cause and no curative treatment, the disease is actually a burden for the patients. Early detection of Alzheimer's and its prodromal stage is very important for possible delay in provision of the disease, and there is thus a great deal of interest in the development of new methods for earlier detection. Structural irregularities in the brain is one of the sensitive feature of the disease (observable on MR images).Deep Neural Network architectures such as Convolutional Neural Network (CNN) has gained a great attention due to its ability to carry out highly discriminative feature representation for classification from images. In this paper, a detailed description about CNN based classification approaches that are designed to accurately classify AD patients from normal ones is presented

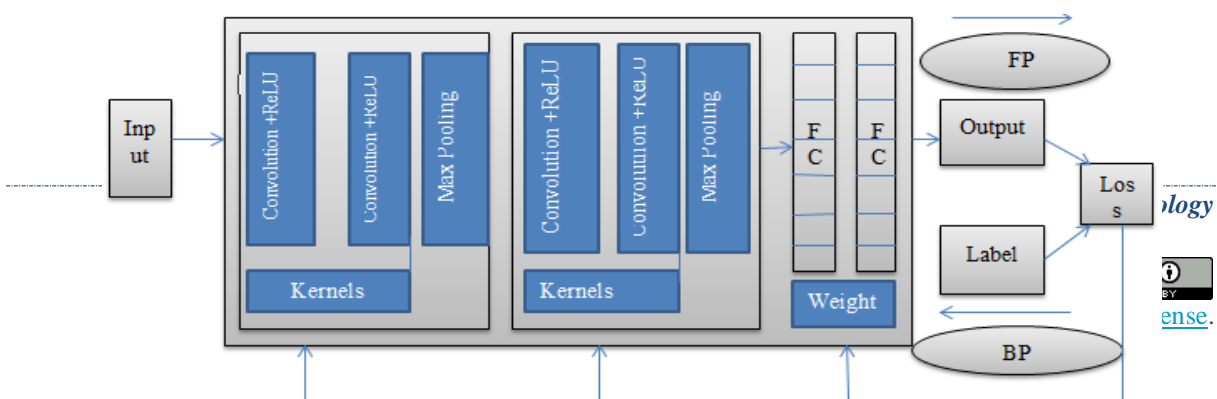
KEYWORDS: Alzheimer's Disease (AD), Deep Learning, Magnetic Resonance Imaging(MRI),Positron Emission Tomography (PET),Multi Imaging Modality.

1. INTRODUCTION

Alzheimer's Disease, a progressive brain disorder mostly occurring in the late life is the most popular dementia in the world .In 2006,the calculable range of individuals with AD was 26.6 million[9].This range is predicted to be over 100 million by 2050.Until now, the reason behind AD remains unknown and no effective treatments are reported to prevent or reverse AD progression. Thus early diagnosis of Alzheimer's disease is of prior importance since it is a very challenging problem because of the immense associated social and economic costs and also for making treatment plans to slow down the progress of the disease.

Alzheimer's disease is associated with progressive brain tissue loss resulting in shrinkage of hippocampus is considered as one of the biomarker of the disease. Voxel-wise, cortical thickness, and hippocampus shape-volume features of MRI[10] are used to diagnose AD. The most extensively utilized imaging modality such as Magnetic Resonance Imaging (MRI) has attracted considerable interest as a tool to identify AD disease biomarkers due to its non-invasive nature in visualizing brain tissues, high resolution and moderate cost. Machine learning approaches using neuroimaging data for developing diagnostic tools have been seeking much attention nowadays. Deep learning being a promising machine learning methodology has made a big loop in identifying and classifying patterns of images ,where Convolutional Neural Network(CNN) being the most widely used architecture of deep learning.

The CNNs were explored to extract the imaging features from MRI [5], for the classification of AD patients from the normal ones. The main strength of CNNs is their ability to extract mid-level and high-level features without much prior knowledge from the raw data. Another benefit of CNNs is that they are easier to train and isdesigned to automatically and adaptively learn spatial hierarchies of features through Forward Propagation (FP) and Back Propagation (BP).



An overview of Convolutional Neural Network Architecture

2. DIFFERENT CLASSIFICATION APPROACHES BASED ON CNN

Compared to other feature extraction techniques, such as texture analysis, followed by conventional machine learning classifiers, such as random forests and support vector machines CNN has achieved much better performance because it does not require hand-crafted feature extraction and also CNN architectures do not necessarily require segmentation of tumors or organs by human experts.

A. ADAPTATION OF 3D CONVOLUTIONAL NEURAL NETWORK (3D-CNN)

The proposed method predicts AD with a deep 3D-Convolutional Neural Network(3D-CNN) which is built upon a 3D Convolutional Auto Encoder(CAE)[11].The concept of the method is to extract features of a brain MRI with a source-domain-trained 3D-CAE and performs task specific classification with a target-domain-adaptable 3D-CNN.Conventional unsupervised autoencoder extracts a few co-aligned scalar feature maps for a set of input 3D images with scalar or vectorial voxel-wise signals by performing data encoding and decoding together[16].Stack of unsupervised CAE with locally connected nodes and shared convolutional weights is being considered because there is no need to learn the global features available due to existence of full connections between all the nodes of the layers in auto encoders.

Training the proposed 3D-CNN consists of pre-training where the convolutional layers for generic feature are formed as a stack of 3D-CAEs,initial training of the lower convolutional layers, and final task-specific fine-tuning. Generic features related to the AD biomarkers, such as the ventricular size, hippocampus shape, and cortical thickness can be extracted by the bottom convolutional layers due to pre-training on the source domain data[7].Net2Net initialization facilitates adapting the 3D-CNN across the different domains based on the target-domain image size and imaging specifications comparison with 3D-CAE.From the experimental results it has been evident that with the proposed method of adaptation[18]by 3D-CNN has gained 97.6% accuracy in classifying AD patients from normal ones.

B. MULTI-MODAL CNN USING LAYER FACTORISATION APPROACH

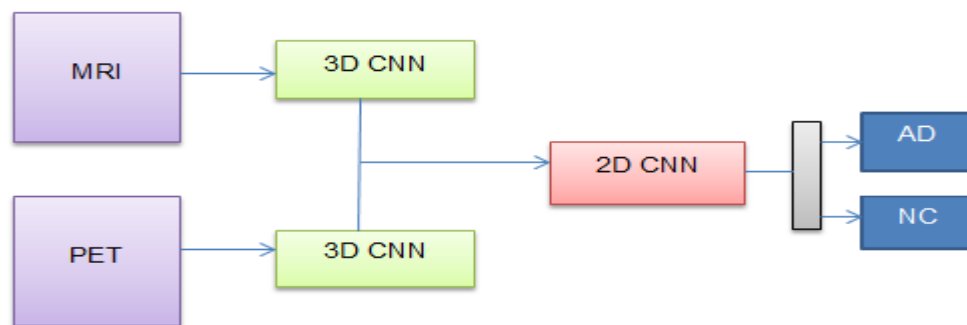
The proposed model enables the simultaneous extraction of high and low level feature representations which is achieved by factorising the convolutional layers in parallel streams. The model takes structural MRI [6] and clinical assessment and genetic (APOe4) measures as inputs. Advantage of multi-modal CNN which use layer factorisation approach is that the number of network parameters while retaining the network depth can be reduced. Descriptive features can be extracted from two types of inputs to the neural network such as a 13-dimensional vector (m) of clinical measures and a 182x218x182 MRI volume through the two sub-networks.

The MRI feature extractor is a 3D CNN[17],and the clinical feature extractor[8] is a series of three fully connected layers. Some of the convolutional layers are split in two before convolving them at the next stage so as to reduce the number of parameters in the latter layer. If the second layer accepts only half of the channels from the previous stage, the overall number of parameters is halved. The network loses some expressive power since the latter layer would only accept part of the feature maps from the previous layer .Thus depth of network increase and training become difficult. So the streams are merged and convolved to achieve information exchange before diverging again. The feature maps obtained from the two sub networks are finally merged and passed on to the fully connected network and the classification task is done. The achieved accuracy in classifying AD groups from normal ones using the proposed method is 98% which makes it more suitable for

data-scarce clinical studies and is less prone to overfitting by making use of the batch normalisation technique which normalises the outputs of each layer, thus accelerating the rate of training.

C. MULTI-MODALITY CLASSIFICATION BY CASCADED CNNs

A Classification method based on the cascaded CNNs to classify AD vs. NC by multi-modality features of Alzheimer's Disease using MRI and PET images is considered [13]. At first for each modality, two deep CNNs are constructed to transform all the informations from brain into compact low to high level features. In the second step a 2D CNN is cascaded to ensemble the multimodality low to high level features for image classification [4] learned from multiple CNN. Multiple deep CNNs trained for each single modality neuroimage is constructed to hierarchically and gradually transform the whole brain image into discriminative features which are extracted at low layers of 3D-CNN, where the upper layers are trained for task specific classification. The output feature maps by 3D CNN of MRI and PET are flattened to one dimension which are then combined into two dimensional feature map to conduct 2D CNN.

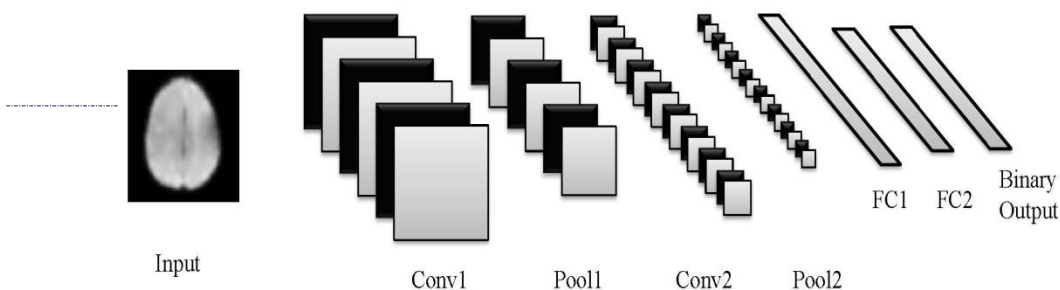


Overview of the Proposed Classification Method Based On Cascaded CNNs.

The benefits of using deep complex architecture is that from a large number of training images it is possible to extract low to high level features. Deep CNNs can take full advantage of the image spatial relationships and learn local 3D filters effectively for the final classification task from the multi imaging modality [15] having different anatomical and functional characteristics. By stacking of multiple modality CNNs the states of Alzheimer's diseases can be presented, finally providing the global class prediction probabilities. The proposed method offers an accuracy of about 89% in effective classification with no segmentation and rigid image registration performed on the MRI and PET scans.

D. CLASSIFICATION USING FMRI DATA AND CNN DEEP LEARNING ARCHITECTURE LeNet-5

By making use of the functional MRI data (fMRI) [2], an effective classification approach is proposed which adopts LeNet-5, a deep learning architecture which was trained and tested with huge number of images allowed to perform feature selection and classification with a unique architecture. By detecting the associated changes in blood flow, fMRI is a technique measuring the brain activity. fMRI sequence can be easily obtained during routine clinical structural MRI session. The silent feature of resting state functional MRI (rs-fMRI) [14] is the ability to measure functional connectivity changes while the patients are not performing any task. LeNet-5 is one of the first shallow Convolutional neural network trained and tested on the MNIST database (Modified National Institute of Standards and Technology database), a large database of handwritten digits that is commonly used for training various image processing systems.



Lenet-5 Architecture Adopted for fMRI data

The LeNet-5 network architecture is comprised of 2 Convolutional layers, 2 Pooling layers, 2 hidden layers and 1 output layer. The non-linearity is added on to the Subsampling layer. Convolutional layer 1 works on all the input feature maps however Convolutional layer 2 takes inputs from a subset of feature maps to generate 16 feature maps by subsampling layer 1 to know the configuration. The partial connections are established rather full connections mainly for reducing the number of weights and for achieving certain level of confirmity in extracting different features as different input features maps. the FC layers. The fully connected layers perform non-linear transformations of these input features and finally the output layer generates outputs to decide the class of the input. The accuracy achieved in the work was 96.86% suggests that the shift and scale invariant features extracted by CNN followed by deep learning classification is most powerful method to distinguish clinical data from healthy data in fMRI.

E. DEMNET: A VGGNET BASED CNN FOR CLASSIFICATION

A 2D Convolution network called DemNet which is a modified version of 16 layer CNN based on the VGGNet architecture[12] that enables successful classification is presented. Better accuracies is achieved without segmenting the gray matter, white matter and cerebrospinal fluid, showing that the classification is independent on prior domain-knowledge and also variations in classifications can be shown with the extracted learned local features[1].The work depicts that 17 coronal slices from the middle part of the brain is sufficient enough to perform classification efficiently.

VGGNet consists of 16 convolution layers and is very promising because of its very uniform architecture. Demnet being a modified version of VGGNet [3] comprises of only 13 convolutional layer and 3 fully connected layer which takes in an input of an MRI slice and crops it to a size of 224×224. The convolution layers were divided into 5 batches by a max-pooling layer which gets maximum value in a region and reduce dimension of inputs and also effectively summarizes the outputs of neighbor groups of inputs as well. The first two batches contain 2 convolution layers while the remaining 3 batches has 3 convolution layers each. Dropout layers are added after each pooling layer to reduce overfitting. Three fully connected layers were used in the network at the end of the last pooling layer, with the number of output neurons being 256-256-2 for the binary classification. The binary classification achieved an accuracy of 98.33% for AD vs healthy controls using the proposed method.

3. PERFORMANCE ANALYSIS

The different approaches being reviewed for the binary classification of AD disease using CNNs have gained varying accuracies and is summarised in table 1. The proposed methods are making use of different data sets and imaging modalities and achieved better performance compared to other deep learning architectures.

Table 1. Summary of CNN based Approaches for binary Classification of AD disease

Author	Modality	Classifier	Accuracy
EhsanHosseini-Asl	Structural MRI (sMRI)	3D-CNN	97.6%
Simon E. Spasov	Structural MRI (sMRI) and clinical assessment	Multi Modal CNN	98%
Manhua Liu	MRI and PET images	Cascaded CNN	89%
SamanSarraf	Functional MRI(fMRI)	CNN based on LeNet architecture	96.86%

Ciprian D. Billones	Structural MRI (sMRI)	DemNet	98.33%
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4. CONCLUSION

Early diagnosis of Alzheimer's Disease (AD) is somewhat very crucial due to associated social and economic burdens for the affected one's. Convolutional Neural Networks have gained astonishing achievements in image classification jobs as it have multi-stream architecture that can accommodate multiple sources of representations of input in the form of channels to the input layer. This paper reviewed various CNN based approaches for classifying AD vs Normal controls using different imaging modalities. Accuracy in classification attained with the reviewed approaches are relatively high but can be further improved by considering some other deep CNN architectures for training and classification.

5. ACKNOWLEDGMENT

We would like to thank our Principal Dr. Jaya V .L and Head of the Department Dr. Gopakumar C for inspiring us to write this paper. We thank all the publishers specified in the reference, who provided insight knowledge for our research and helped to publish our work in this conference.

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