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Automated detection of Alzheimer's Disease using Deep Learning in MRI

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Abstract. Alzheimer's disease (AD) is a progressive mental deterioration and incurable neurodegenerative disease that can occur in middle or old age, due to generalized degeneration of the brain. Because of the irreversible nature of the progression of Alzheimer's disease, the early diagnosis of AD has an immense clinical, social, and economic need. This research output proposing a state-of-the-art, easy, and early automated deep learning-based system to predict AD from a large MRI dataset of normal and diseased subjects. It classified the database of 111 subjects into Mild Cognitive Impairment (MCI), Alzheimer's disease (AD), and Normal classes. Classification tools like Support Vector Machines (SVM) and different models of Deep Neural Network (DNN) algorithms were tested. Deep learning algorithms were offering high accuracy of about 80-90% on AD prediction. For the prediction of diseases such as Alzheimer's, Dementia, and Parkinson's, applying highly accurate computational - automated machine learning - tools will help to diagnose the disease in the early stage itself and provide a better clinical, social and economic outcome.

Keywords— Alzheimer's disease, Image classification, Transfer learning, MRI, ReLU

1. Introduction

Alzheimer's disease (AD) is a chronic condition that causes the shrinking of brain and brain cells to die. Due to generalized degeneration of the brain, it can occur in middle or old age. AD is the cause of about 60–70% of cases of dementia. Short-term memory loss is the most common early symptom of this disease. Problems with language and behavior, disorientation, mood swings, loss of motivation, and inefficiency in managing self-care are seen when the disease advances. As a person's condition declines, they often feel emotional and psychological problems from family and society. As the disease progress, bodily functions are lost and ultimately the patient will lead to death. Although the speed of progression of the disease can vary, the average life expectancy after diagnosis is less than nine years [1], [2].

Around worldwide 29.5 million people approximately suffered Alzheimer's disease in 2015. At the age of 65, it is most often begins in people, but 4% to 5% of cases are early-onset before these ages. Due to the cause of Dementia, 1.9 million deaths in the year 2015. AD is one of the most financial diseases in developed countries. In India, some form of Dementia is suffering by more than 4 million people. In 2050, the number of people suffering from AD will set to triple [1].

There are medical treatments that are available to solve the disease effect in the early stages of AD. But due to the irreversible nature of the progression of Alzheimer's disease, the early diagnosis of AD has an immense clinical, social, and economic importance. The advancements in imaging and computational technologies helped medical science to identify the disease in its early stage and start the remedial clinical procedures. But still, there is a demand for accurate and high-speed computational methods and

algorithms for the easy and early diagnosis of neurological disorders. AD introduces both structural and functional changes in the brain. It creates dynamically evolving morphological and anatomical patterns. By investigating such changes qualitatively and quantitatively and comparing them with the normal activities and features of the human brain helps to find out the new changes created by AD.

Based on the morphological and anatomical changes, the Alzheimer's and Normal cases are classified as AD (Alzheimer's disease), MCI (Mild Cognitive Impairment), and NC (Normal Control) subjects, where MCI is an intermediate stage in between AD and Normal Controls. Therefore the quantitative and qualitative diagnosis of AD is of high value in clinical practices since it can solve more time for the treatment and then improve the quality of life of the patient and their caretakers.

The current state-of-the-art diagnosis methods have limited power in clinical practices owing to various technical and clinical issues. Moreover, only a limited set of methods are specifically designed for the early prediction of AD. This work proposes a state-of-the-art easy and early diagnosis scheme using Magnetic Resonance Images (MRI) with the help of advanced machine learning tools and algorithms such as deep learning. This work proposes an automated (machine learning) system to predict AD from a dataset of normal control subjects and diseased subjects. It classifies the data into Normal, Mild Cognitive Impairment (MCI), and Alzheimer's disease. It helps a radiologist or clinical practitioner to easily predict the given MRI image belongs to which category with a high accuracy level than the conventional classification – prediction system.

2. Materials and methods

2.1. The model

A typical MR Image-based classification and prediction algorithm have shown in the literature as shown in Fig. 1. This model contains the training and testing data sets, pre-processing stages including filtering, skull stripping *etc.,* and feature extraction for classification and prediction stages. In most of the recent works of literature under the title of classification and prediction, this approach is followed. The major disadvantage of this method is the time consumption due to computational complexity and relatively lower accuracy rate [3], [4], [5].
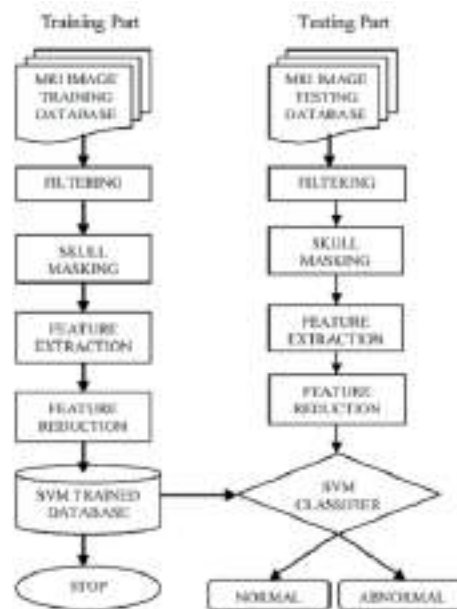

Figure 1: Typical MRI based classification model [7]

The new approach designed in this work using the deep learning algorithm, as represented in Fig. 2 will eliminate the pre-processing stages and thereby reduces the computational complexity and improves the overall performance in time and accuracy in comparison with the conventional models. That is the

deep learning algorithm does not require any pre-processing stages if we can provide the necessary and sufficient requirements to process with the deep learning technology.
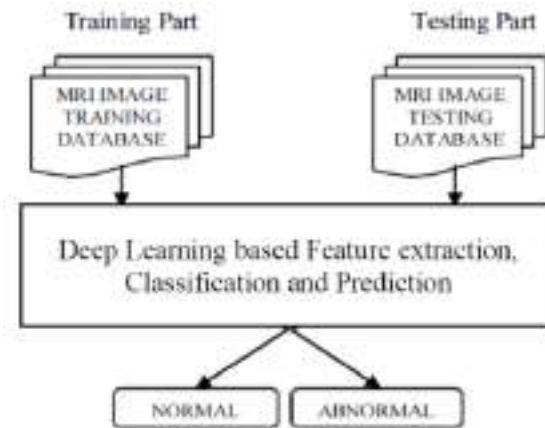

Figure 2: Proposed deep learning-based classification model

The high accuracy rate makes deep learning state-of-the-art. After 2012, with the help of deep learning technology, there was a considerable improvement in the accuracy level, as shown in the Fig. 3 is the error rate plot of Image Net Large Scale Visual Recognition Challenge (ILSVRC) . The improvements in computational efficiency, availability of large datasets of labeled and classified data, and Convolutional Neural Network (CNN) models made deep learning more attractive in classification and prediction problems. The possibilities of deep learning models in medical image processing applications - especially in image-based prediction problems – are not fully explored.
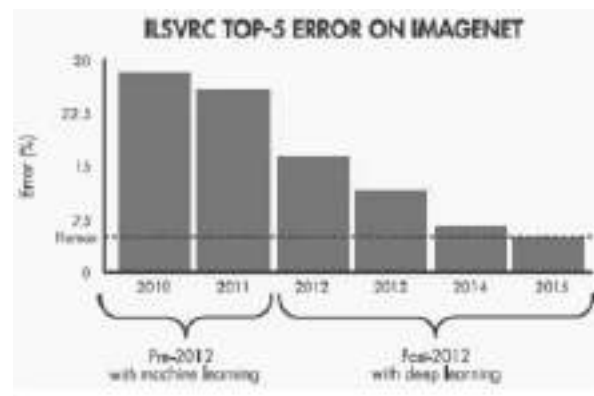
Figure 3: Error rate in deep learning [9]

This work is an attempt to classify the diseased and normal subjects and predict Alzheimer's disease. The goal of this work is to design and implement an automated machine (deep) learning system for the prediction of Alzheimer's disease. Classification and prediction were the two major computational tasks in this problem. The three aspects of a typical neuro-inspired machine learning system have implemented as:

(i) Modeling of neural activities in the brain – which had been recorded by functional Magnetic Resonance Images (fMRI).

(ii) Analysis of neural data has been done in the classification and feature extraction process of MR Images.

(iii) Neuro-inspired learning algorithms have been designed and implemented using the transfer learning technique of pre-trained deep neural networks.

2.2. Data

The MR Images for the examination have been procured from the ADNI (Alzheimer's Disease Neuroimaging Initiative) data set of the University of Southern California. For the early diagnosis and follow-up of Alzheimer's disease, ADNI is a continuing, longitudinal, multi-study intended to create clinical, imaging, hereditary, and biochemical biomarkers.

The ADNI works began in 2004 and included 200 subjects diagnosed with early Alzheimer's disease (AD), 400 subjects with Mild Cognitive Impairment (MCI), and 200 elderly normal control subjects. For imaging assortment and examination for applications in clinical practices, ADNI is committed to building up standardized methods. ADNI MRI core beginnings with the ADNI-1 project for the first five years (from 2005 to 2010). ADNI sample picture of an MCI subject is shown in Fig. 4.
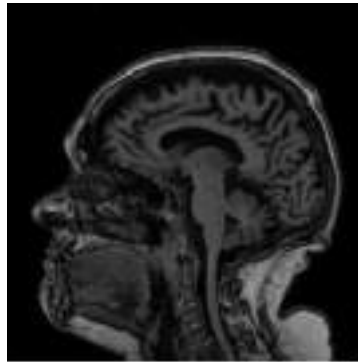

Figure 4: ADNI MRI sample image of MCI subject

ADNI database provides standardized images, which can be directly used for the training and testing of the classification-prediction model. On account of MR images, all subjects who took on the ADNI-1 stage undergone a 1.5T protocol scanning at multiple point times. It differed by baseline clinical findings at 0, 6, 12, 24, and three years for MCI, AD, and Normal Control subjects. ADNI-1 finished in October 2010 and the subsequent stage, ADNI-2 (ADNI-GO) for the following 5 years of ADNI going through 2015.

The Alzheimer's Disease Neuroimaging Initiative Project provides us a large and great database of MR images that are used in this work. Normalized MR images of 46 MCI, 25 AD, and 40 Normal Controls as a total of 111 subjects having a data volume of 25 GB downloaded from the ADNI-2 library and which has been used as the database. The downloaded files were of '.nii'. *i.e.,* the NIfTI (Neuroimaging Informatics Technology Initiative) format. The NIfTI files were converted to JPEG format and 70-100 high-quality JPEG images were selected from each NIfTI file. The JPEG image database having enough images of MRI, AD, and Normal Controls was used for the training of neural networks.

2.3. Computational requirements

Depending on the data size and computational capability, the deep learning model training may take time from hours to weeks. The computation option available is of three types (CPU-based, GPU-based, and cloud-based). CPU-based computation is the readily available and simplest option, but it is very slow in performance. But, a GPU reduces the training time very much.

A high-performance computer supporting CUDA Graphical Processing Unit (GPU) has to be used to process the large volume of MR image data. Generally, NVIDIA GPU with computing capability above 3.0 is highly recommended for deep learning applications. Multiple GPUs can speed up the time for the training process even more.

NVIDIA GEFORCE GTX 1050 GPU with computing capability 6.1 supported by CUDA 9.2 driver has been used in this work for the high-speed processing and training of the MR image database. GPU specifications were shown in Table 1.

Table 1: GPU specifications

	NVIDIA GeForce GTX 1050'
Compute capability	6.1
Driver version	9.2000
Toolkit version	8
Multiprocessor count	5
Clock rate KHz	1493000
Total memory	4 GB

NVIDIA made a parallel computing platform and Application Programming Interface model (API) known as CUDA (Compute Unified Device Architecture). For general purpose processing, the CUDA-based Graphics Processing Unit to utilize for general-purpose processing is termed as GPGPU (General-Purpose Computing on Graphics Processing Units). Likewise, for the implementation of computer kernels, the software layer of CUDA gives direct admittance to the GPU's virtual instruction set and parallel computational elements.

3. Deep learning

Deep learning is a kind of AI where a model figures out how to perform the classification problems directly from the given dataset, which might be pictures, text, or sound. Deep learning is typically actualized by neural network architecture. As the number of layers turns out to be more, the network will be deeper. As contrasted with the conventional neural networks containing 2 or 3 layers, the deep neural networks can have many layers. Deep learning models are particularly appropriate to identification applications of artificial intelligence such as computer vision, face recognition, natural language processing, voice recognition, social media filtering, and bioinformatics. It has delivered results equivalent to and now and again better than human experts [4], [9].

Accuracy makes deep learning state-of-the-art as compared to other machine learning tools. This high degree of accuracy has been enabled by the advancements in the three technological areas.

(i) Easy and free availability of large datasets (such as ImageNet, Caltec101, MNIST), gave access to massive sets of labeled data.

(ii) High computing power with the help of high-performance GPUs. It will boost the training of a large set of data needed for deep learning and reducing the training time.

(iii) Pre-trained deep neural network models.

With the help of the transfer learning technique, the pre-trained deep neural network models (such as AlexNet, VGG-16, Resnet-50) can be retrained to perform new classification and pattern recognition tasks [4].

4. DNN architecture & transfer learning models

The sufficient resources for the functioning of the deep learning model have provided as:

(i) The labeled data of functional Magnetic Resonance Images (fMRI) from the ADNI database.

(ii) The high-performance GPU supported by CUDA – MATLAB platform.

(iii) Pre-trained deep neural network models such as AlexNet, VGG-16, VGG-19, and GoogleNet.

The dataset of MR images contains several images of one of the three categories: AD (Alzheimer's disease), MCI (Mild Cognitive Impairment), and NC (Normal Control) and the deep neural network needs to automatically recognize a random MR Image is in which category. The images are labeled for training the network. With the help of this training data, the deep neural network would then be able to start to comprehend the MR Image's specific features and partner them with the respective group of data. Each layer in the network takes the data from the past layer, transforms it, and finally passes it on to the next layer. The network will increase the complexity and detail of what it is learning from layer to layer. The most important characteristic of the deep learning model is its self-learning capability. *i.e.,* the network will learn directly from the data given. Therefore, what features are being learned and the number of such very minute features do not influence the human.

Deep Neural Network architecture has two important sets of layers. The former is feature detection layers and the latter is classification layers. The feature detection layers in the network perform convolution, pooling, and Rectified Linear Unit (ReLU) operations on the data. Convolution puts the input MR images through a set of convolutional filters. Every one of them activates certain significant features from the MR images. Pooling simplifies the output by performing nonlinear downsampling and so that reducing the number of parameters that the network needs to learn. ReLU permits quicker and more effective training by mapping negative qualities to zero and keeping up positive values.

Rectified Linear Units (ReLU) is an activation function introduced by Hahnloser *et al.,* in 2000, with strong biological and mathematical justifications. In 2011, it was demonstrated for better training of deep neural networks as compared to the widely used logistic sigmoid activation functions. As of 2018, ReLU is the most popular activation function for deep neural networks [13].

It works by thresholding values at 0. It outputs 0 when $x_1 < 0$, and conversely, it outputs a linear function when $x_1 \geq 0$.
i.e.,

$$f(x_1) = x_1^+ = max(0, x_1) \tag{1}$$

where x_1 is the input to the neuron [6]

These three operations - convolution, pooling, and ReLU - were repeated over tens or hundreds of layers, with each layer learning to detect different features. After the feature detection layers, the DNN architecture shifts to classification layers. It has a Fully Connected (FC) layer and a final layer with classification results. The FC layer outputs a K dimensional vector, where K is the number of classes that the network will be able to predict. The value of K is equal to 3 in this classification problem. (NL, AD, and MCI). This vector contains the probabilities for each class of any image being classified. The final layer of the DNN architecture uses a softmax function to provide the classification output.

The softmax function provides a discrete probability distribution for K classes (here $K=3$). *i.e.,*

$$\sum_{k=1}^{K} P_k \tag{2}$$

If x_1 is the activation function at the penultimate layer of the network and θ is its weight parameter at the softmax layer, then the input to the softmax layer is:

$$S = \sum_{i}^{n-1} \theta_i x_i \tag{3}$$

and

$$P_K = \frac{exp(S_K)}{\sum_{i}^{n-1} exp(S_K)} \tag{4}$$

Then the predicted class will be

$$\hat{y} = argmax P_i; \quad i \in 1, 2, ... N \tag{5}$$

5. Results and discussion

As referenced before, the MRI classification and prediction task utilizing DNN architecture has implemented by transfer learning technique. Transfer learning is a methodology that applies knowledge on one kind of problem to a different but related problem in AI. This technique delivers the most accurate results, yet it requires a huge number of labeled data and powerful computational requirements. The transfer learning using pre-trained deep network models, such as Alexnet, VGG, and GoogleNet were performed and evaluated.

In most of the classification-prediction problems on medical images has been implemented with Support Vector Machines (SVM). Here SVM and deep learning models were compared and investigated the performance. Based on the classification accuracy and prediction responses, deep learning is coming as the most convenient tool for pattern recognition and prediction problems, if enough set of resources are provided.

SVM based classifier was giving the result with 70-80% accuracy but DNN models have the prediction accuracy of 80-90% as represented in Fig. 5. A conventional classification model will take much time for training and testing, where as the evaluation of DNN Models on GPU supported by CUDA has given relatively small processing time. The accuracy level and response time can be improved further if we can provide much more data and a better computing platform as shown in Table 2.

Table 2: Model V/c Accuracy chart

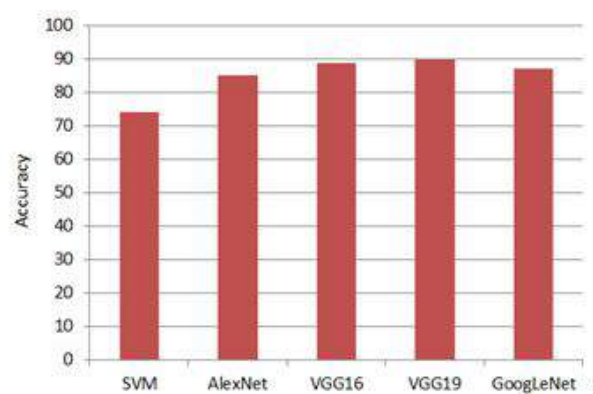| Classification – Prediction model accuracy	Accuracy			
	MCI	AD	NC	Total
SVM	0.7017	0.8366	0.6891	0.7425
Deep learning with AlexNet	0.8760	0.7600	0.9177	0.8514
Deep learning with VGG16	0.8568	0.9147	0.8961	0.8892
Deep learning with VGG19	0.9287	0.8679	0.9041	0.9002
Deep learning with GoogLeNet	0.8938	0.8754	0.8497	0.8729

Figure 5: Accuracy v/s DNN model plot

6. Conclusions

An automated machine learning tool for the prediction of Alzheimer's disease using a deep learning algorithm has been successfully designed and implemented by this work. The performance levels of SVM and DNN models were also examined. Deep learning shows high accuracy level of about 80-90% in Alzheimer's disease prediction.

The method suggested in this work will solve social and economic problems of AD, if it is successfully implemented in clinical practices. At present, the clinical trials of computational techniques are very limited. For the prediction of diseases such as Alzheimer's, Dementia, and Parkinson's applying highly accurate computational - automated machine learning - tools will helps to diagnose the disease in the early stage itself and reduce the treatment time.

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