Detection of Alzheimer’s Disease using CNN Architectures

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Abstract*: *Alzheimer’s disease is a neurological condition that causes some structural alterations in the brain. In this paper we have given an overview of all the available good CNN models used in medical imaging for image classification purpose such asAlexNet, GoogleNet, ResNet 18, ResNet 50, SqueezeNet and DenseNet. Using these CNN models, we have been able to classify three different stages of Alzheimer's disease – Cognitively Normal (NC), Mild Cognitive Impairment (MCI) and Alzheimer’s Disease(AD). The dataset is derived from ADNI and has been preprocessed before applying various CNN models. The experimental results demonstrate that all models performed well and the best accuracy has been acquired by the GoogleNet of 96.81%.

***Keywords*-Alzheimer’s Disease, Deep Learning, Convolutional Neural Network**

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I. INTRODUCTION

The field of Artificial Intelligence works as an engine with great potential in all the fields around us including health industry. One of the biggest advantage and reason for bringing up AI in health industry today is the availability of huge amount of medical data. In recent years AI has used the available datasets for analysis and it has laid an impact on the fields like Drug discovery [4], finding the extent of risk of a patient, Radiological imaging, Pathology, Dermatology etc. Based on the datasets various models can be trained and tested to create a benchmark for various health issues and huge amount of data can be analyzed without getting tired or any human error. One such example of a form of dementia that can be detected from its dataset is Alzheimer’s disease.

Alzheimer’s disease is a neurological condition for which presently no therapy or cure is known. It is a kind of dementia that causes certain structural alterations in the brain. There occurs loss of neurons and synapses that brings some noticeable changes in brain tissue and can be detected using structural MRI images. One of the reliable ways to detect this problem is by using Machine Learning models for carrying out analysis of neural data where various pattern recognition tasks can detect the brain activities and after which measures can be taken to slow down its progress. Many models have been employed along with time for neuroimaging and a subfield of machine learning proved to be the best among others which is called Multivoxel Pattern Analysis[6]. MVPA is a technique that studies a neural paradigm and finds out the information contained in it [6]. MVPA have been implemented using various machine learning techniques among which the most used technique was Support Vector Machine that gave very good results in detection of various mental illnesses. Like SVM when associated with other ML techniques achieved high accuracy in diagnosis of AD [1]. Similarly MVPA was implemented using SVM in many contexts and gave promising results.

However, Machine Learning requires manual selection of features in an image. For underdeveloped regions, feature selection might prove to be a tedious and difficult task. So to tackle this issue Deep Learning came into use that does not require any preparatory information about the image and can extract features on its own using its deeper layers[7]. The subclass of deep learning that can deal with imaging efficiently is Convolutional Neural Network. CNN has given promising results in pattern recognition in the past few years. A comparison between various CNN models (AlexNet, ResNet-18, ResNet-52, GoogleNet, SqueezeNet, DenseNet) on detection of Alzheimer’s Disease have been made and discussed in this paper.

The remaining part of the paper has been organized as follows- Section 2 describes the related work, Section 3 mentions the proposed method, Section 4 explains the experiment and result, and finally Section 5 concludes the paper.

II. RELATED LITERARURE

In past few years researchers have worked on finding ways of detecting AD efficiently. Plenty of remarkable work has been done in this field. AB Rabeh et al. [1] applied SVM for detecting the disease and used three sections of the brain – Hippocampus, Corpus Callosum and features of Cortex for it. Imaging and biological data consisting of MRI and FDG-PET scans from ADNI were classified using a multi-modal approach that used random forest-derived similarities [24]. In due course of time Deep Learning gained much importance as it gave better results and a comparison was given by P.Baglat et al.[10] where they compared their CNN model results with the results of ML algorithms and found that deep learning works better and give good results by requiring huge amount of data. S.Bringas et al.[22] used patient mobility information to predict stage of AD using CNN and compared it with traditional feature based classifiers(Decision Trees, k-Nearest Neighbours, Logistic Regression, SVM) where CNN gave improved results over standard feature based models. E.Hosseini et al.[25] used 3D CNN for diagnosing AD. S.Kloppel et al.[23] gave a way of starting computer based diagnostic for clinical applications by using SVM and detecting AD.

III. PROPOSED METHOD

A. Preprocessing

Preprocessing converts unstructured data into a usable format. In this project we have used SPM (Statistical Parametric Mapping) [8] which is a free and open software for neuro-imaging. Here, following steps were followed for preprocessing – *Realignment* to arrange all the slices in same orientation and remove the misalignment, *Slice time Correction* to adjust all slice of a single volume in time to achieve the desired result with respect to one reference slice and *Normalization* to bring all the images in same 3D space defined by MNI template followed by *Segmentation* which was implemented using Python.

B. Segmentation

Image segmentation in the field of medicine is critical in a variety of situations where computer-aided diagnosis tools are used. In reference to MRI brain images, segmentation is normally used to determine and visualize the anatomical structures of the brain, to analyze brain changes and to carve out active regions. Clustering in neuro-imaging is critical for the accuracy of detection of disease in brain, its diagnosis, and treatment effectiveness. The brain anatomy is complicated, and correct segmentation of the brain tissues is required for accurate detection of several brain illnesses. For segmentation, we have used k-means clustering. Since the images were 4D images so here a python library nibabel [27] has been used to read the image and convert it into a matrix because of which the intensity value of pixels of image has been stored as integer values in matrix.After this, clustering has been done on images. Since it is difficult to handle.nii images, so for easy viewing and handling the images after clustering the MRI scans have been converted into .jpg images.

The clustered images are ready to use but there may be some redundant information present beside the main brain tissue in the image so the brain tissue has been taken out from the raw image and all the irrelevant regions have been removed in this step as shown in Figure 1.

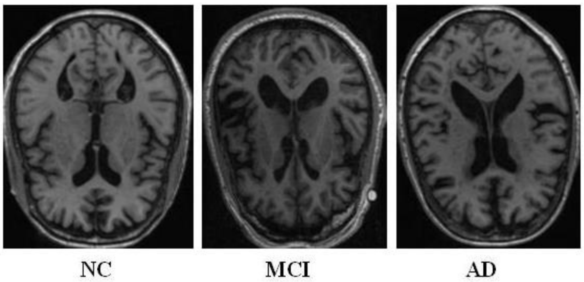

Fig. 1. MRI scans after preprocessing

C. Methodology

After Image Segmentation, feature selection and extraction is required as MRI images consists of many voxels (features) and it becomes important to remove the redundant features. This improves the model's learning time, prevents curse of dimensionality [9] and reduce the modeling cost. If this is done automatically without the user input of features then the model will become more accurate and fast and for this purpose we have used Deep Learning in our experiment. In Deep Learning, most famous successful model for imaging is Convolutional Neural Network. In past few years it has given very good results in pattern recognition problems and many diseases and activities of brain have been traced using CNN like brain tumor classification [11], detection of Alzheimer's disease as MCI/AD/CN [10], identifying biomarkers for conduct disorder in children and adolescent[12].

CNN is basically a mathematical tool of convolution used for matrices. It uses filters of size smaller than input images to be multiplied repeatedly by the pixel values of image to give good feature extraction results. It does not require any information beforehand for feature extraction [13]. For example- In brain image analysis we do not need to know beforehand that what parts of brain will be affected in a cognitive event and where they are located in the image [14].

There are following layers in CNN:

1. *Convolution Layer*: Basically in CNN process various set of filters having their own application (such as edge detectors, sharpening, blurring) are multiplied to the filter sized part of input image and then the final value is found by summing up to a single value[15]. The filters used are smaller in size than the image so that it can be multiplied by the input patches repeatedly to get efficient feature extraction. Output of this process yields a "feature map". There can be many feature maps possible each extracting one feature. Example- Consider an image of size 10 x 10 and filter of size 3 x 3 then the output of this layer will be an 8 x 8 image. However, during this process of convolution some information gets lost and also there is less usage of the information of pixels on the border of the image so their contribution is reduced in feature selection and to handle these issues "Padding" is used where a row and column of zeros are added on the border of the image. Another aspect that can be added to convolution layer is "Stride". It is used for compressing the images [14].

2. *Pooling Layer*: Output of convolution layer may have some overlapping that results in carriage of redundant information [16]. To facilitate this pooling layer is used that keeps the main information and reduces the resolution of the feature maps[17]. Number of filters remain the same and parameters reduces which further reduces the complexity. There are two common types of pooling methods: Max pooling and Average pooling.

3. *Fully Connected Layer:* The output of the final pooling layer is Flattened into a vector and given as input to this layer where it connects each node in one layer to every node in another layer. After this, Softmax activation function is used which converts the weighted sum value into number of probabilities. These probabilities tells the classification membership [18].

After preprocessing of the MRI scans the whole implementation has been carried out on AncondaJupyter Notebook. The whole dataset have been split into 70% as training set, 15% as validation set and 15% as test set. Then, most of the famous CNN models available have been trained from scratch for 100 epochs to make the model ready to detect AD and at the end accuracy of each model has been obtained.

For the proposed method, the following CNN Architectures have been considered:

i. *AlexNet*: It is a famous architecture according to which CNN is better than standard feedforward network whose capacity can be varied and make better assumptions about images to be classified. It consists of 8 weighted layers where first 5 layers are convolutional layers and last 3 are fully connected layer. Along with this, it uses ReLU non-linearity that improves the training performance [19].

ii. *GoogleNet*:Szegedy et al.[20] from Google designed the ILSVRC 2014 winner. To decrease the number of parameters in this design, an Inception module is used. Furthermore, instead of completely linked layers at the top of convolutional layers, it employs a pooling layer. The inception module's concept is that instead of picking one convolution filter, we can employ all of them at once. To put it another way, it process the particular input along with numerous convolution filter(1x1, 3x3, 5x5) and also applying pooling. Finally, outcomes of all of these procedures are combined.

iii. *ResNet:* This architecture won the top 5 error rate of 3.57%. It addresses the problem of accuracy degradation which is the problem where accuracy reduces when depth of the network increases. They gave this architecture which introduced residual block that used the concept of Identity mapping. Identity mapping adds the output of a previous layer to the output of the next layer. It considers that if there exists a network with lesser layers and identity mapping layers are added to it with letting other layers learn from shallower model then the training error will be approx. the error of the shallower network [3]. Based on the number of layers many models of ResNet are available – ResNet-18 ResNet-34, ResNet-50, ResNet-101, ResNet-152. ResNet-18, ResNet-34 consists of two layer blocks and ResNet (50, 101,152) consists of three layer blocks and are better than the latter in terms of accuracy. Here, we have used ResNet-18 and ResNet-50.

iv. *SqueezeNet*: This is a model that basically deals with parameter reduction along with achieving good accuracy level. It has used concepts like using 1x1 filter instead of 3x3 filter, using squeeze layers to reduce the number of input channels to 3x3 filters and producing large activation maps to get high accuracy for reducing the parameters along with maintaining good accuracy [2]. It consists of two convolutional layers; one at the beginning and other at the end and eight Fire Modules that are the building blocks of this model. Initially a learning rate of 0.04 is considered and then it linearly increases. This model's accuracy is equivalent to that of AlexNet with 50 times less number of parameters.

v. *DenseNet (Dense Convolutional Neural Network)* : It is an advancement over CNN models in terms of number of layers which states that a normal a layered CNN model has L connections and DenseNet is an improvement over it where it has a L(L + 1)/2 connections. The model is like each layer's feature map is concatenated and given to next layer facilitating the concept of DenseNet where each layer is the feature map of all the layers preceding it as input. This concept of model improves the efficiency and information flow. Whole architecture consists of dense blocks having a transition layer between them for carrying out convolution and pooling[21]. This model saves itself from learning of the irrelevant features by using less parameters.

IV. Experimental Results & Discussion

The data is acquired from ADNI (Alzheimer's Disease Neuroimaging Initiative). The dataset consists of MRI (T1w) scans of people with the average age greater than 70 years. Since one of the main requirements of deep learning is large amount of dataset, so the data is derived from 2 sources in ADNI which has made our work more robust. After combining data derived from 2 sources overall dataset consisted of 2934 MRI scans. The participants were in various stages of sickness based on their MMSE. ADNI categorizes the participants into 3 classes of Cognitively Normal (NC), Mild Cognitive Impairment(MCI) and Alzheimer's Disease(AD). Overall we had : CN : 967, MCI : 985, AD : 982. The downloaded images were in .nii extension i.e. NIFTI format.

TABLE I: PERFORMANCE OF THE MODELS BASED ON ACCURACY

CNN Models	Validation Accuracy	Test Accuracy
AlexNet	95.46	96.59
GoogleNet	95.01	96.81
ResNet 18	94.78	95.01
ResNet 50	95.69	96.13
SqueezeNet	95.23	94.09
DenseNet	95.59	94.54

The methodology consisted of 2 phases –

a) Preprocessing which converted the images into usable format that was given as input to CNN models

b) Training and Testing Phase that made the model ready to detect AD. A set of learnable filters was used in all the models to extract low to high level features from images and a total of 100 epochs with batch size 16 (i.e. for each epoch we had 2053/16 = 129 images) were executed.

Figure 2 depicts the accuracy graphs of all CNN models where each graph has number of epochs on x-axis and accuracy on y-axis. GoogleNet's graph is accompanied with accuracy plot of Auxiliary classifier.

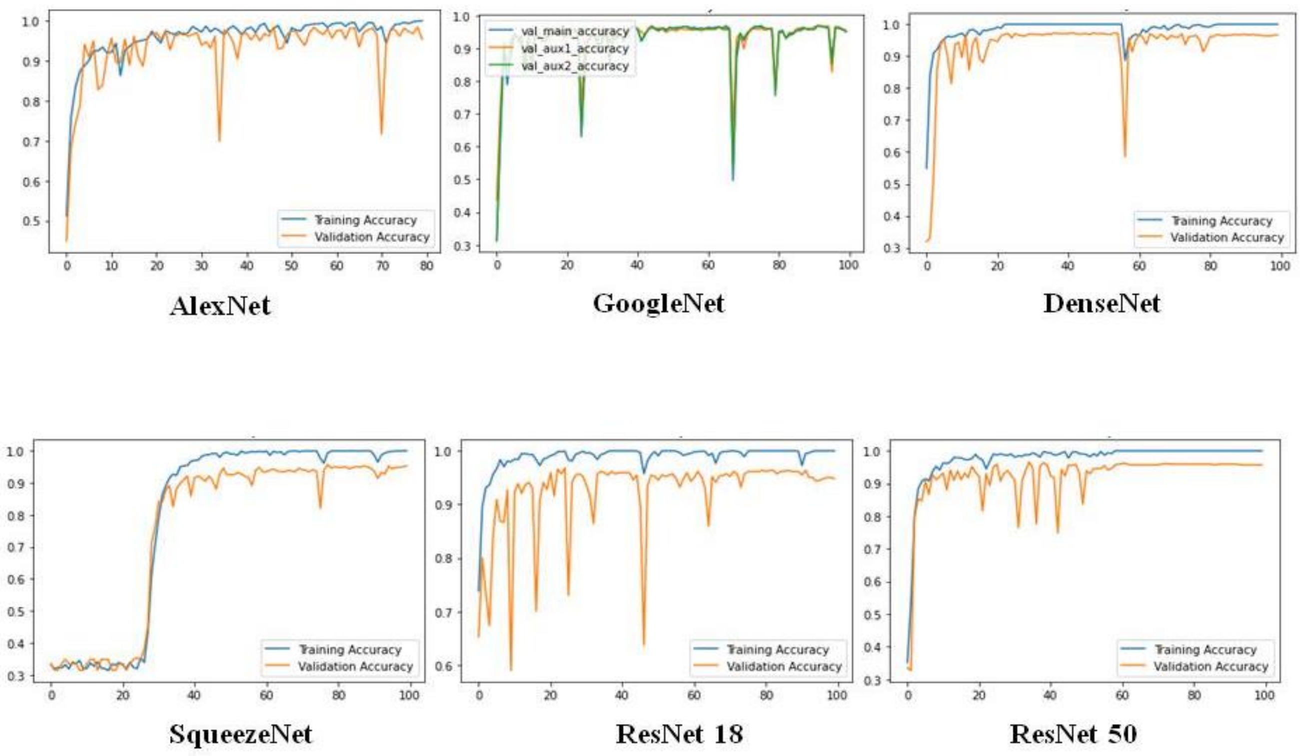

Fig. 2. Accuracy Graphs of all CNN models

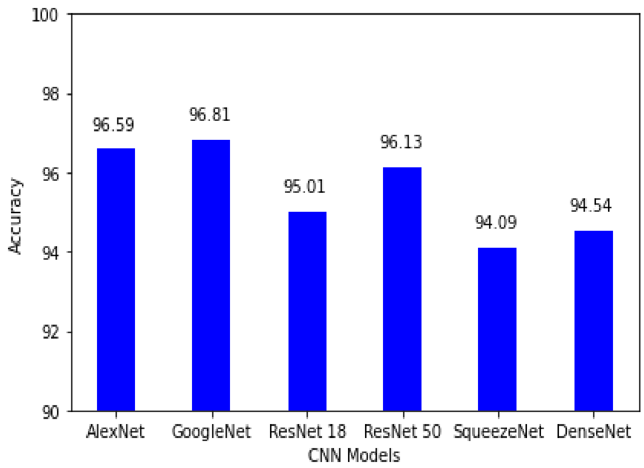

Fig. 3. Comparison of performance of all famous CNN Models

V. CONCLUSION

In this paper, an overview of different CNN models used in medical imaging for image classification has been discussed. This paper utilizes different CNN models for the detection of Alzheimer's disease. The experiment has been conducted on dataset derived from two sources in ADNI. The experimental results demonstrate that the GoogleNet achieves higher accuracy as compared to the other CNN models in classifying the three classes of AD, NC and MCI. The experimental results reveal the effectiveness of deep-learning techniques in the detection of Alzheimer's disease. The proposed method can be further improved by incorporating other features along with deep learning models in order to produce higher accuracy.

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REFERENCES

[1] A.B. Rabeh, F. Benzarti and H. Amiri, "Diagnosis of Alzheimer diseases in early step using SVM (Support Vector Machine)," 2016 13th International Conference on (CGiV), 2016, pp. 364-367

[2] F.N.Iandola, S.Han, M.W.Moskewicz, K. Ashraf, W.J.Dally and K.Keutzer, "SqueezeNet: AlexNet-level accuracy with 50x fewer parameters and <0.5MB model size",2016, arXiv:1602.07360 [cs.CV]

[3] K. He, X. Zhang, S. Ren and J. Sun, "Deep Residual Learning for Image Recognition," 2016 Comput Soc Conf Comput Vis Pattern Recognit , 2016, pp. 770-778

[4] Justin S. Smith, Adrian E. Roitberg, and Olexandr Isayev, "Transforming Computational Drug Discovery with Machine Learning and AI," ACS Medicinal Chemistry Letters **2018,** vol. 9 Issue 11, pp.1065-1069

[5] Z.Akkus, A. Galimzianova, A. Hoogi, D.L.Rubin and B.J.Erickson,"Deep Learning for Brain MRI Segmentation: State of the Art and Future Directions", J Digit Imaging vol. 30, pp. 449–459 (2017).

[6] A. Mahmoudi, S. Takerkart, F. Regragui, D. Boussaoud and A.Brovelli, "Multivoxel Pattern Analysis for fMRI Data: A Review", Comput. Math. Methods Med., 2012, pp. 1-14

[7] X.Tang, The role of artificial intelligence in medical imaging research, BJR|Open, vol. 2, Issue 1November 2020

[8] W. Penny, K.Friston, J. Ashburner, S. Kiebel and T. Nichols, "Statistical Parametric Mapping: The Analysis of Functional Brain Images".

[9] R.Bellman,"DynamicProgramming",Science,1966, vol. 153,no 3731, pp. 34-37

[10] A. W. Salehi, P. Baglat, B. B. Sharma, G. Gupta and A. Upadhya, "A CNN Model: Earlier Diagnosis and Classification of Alzheimer Disease using MRI," 2020 International Conference on Smart Electronics and Communication (ICOSEC), vol. 2020, pp. 156-161

[11] Z.N.K. Swati, Q. Zhao, M. Kabir, F.Ali, Z.Ali, S.Ahmed, and J.Lu, "Brain tumor classification for MR images using transfer learning and fine-tuning", Comput. Med. Imaging Graph., vol. 75, 2019, pp. 34-46

[12] J.Zhang , X.Li, Y.Li, M.Wang, B.Huang , S.Yao and L.Shen, "Three dimensional convolutional neural network-based classification of conduct disorder with structural MRI", Brain Imaging Behav. vol. 14 no 6,2020 Dec; pp. 2333-2340.

[13] Y. LeCun, P. Haffner, L. Bottou and Y. Bengio (1999),"Object Recognition with Gradient-Based Learning. In: Shape, Contour and Grouping in Computer Vision", Lecture Notes in Computer Science, vol. 1681. Springer, Berlin, Heidelberg, pp. 319–345

[14] S. Albawi, T. A. Mohammed and S. Al-Zawi, "Understanding of a convolutional neural network," Int. Conf. Eng. Technol(ICET)vol.2017, pp. 1-6,

[15] X. Wang, X.Liang, Z.Jiang, B.A. Nguchu, Y. Zhou, Y.Wang, H.Wang, Y.Li, Y.Zhu, F.Wu, J. Gao and B.Qiu, "Decoding and mapping task states of the human brain via deep learning", Hum. Brain Mapp, vol. 41, Issue6, pp. 1505-1519, April 15, 2020

[16] J. Peng, "Understanding of the Convolutional Neural Networks with Relative Learning Algorithms." vol. 2018, pp. 657-661

[17] S.D., A.C.Müller,S. Behnkeand D.Scherer, "Evaluation of Pooling Operations in Convolutional Architectures for Object Recognition", Artificial Neural Networks – ICANN 2010. vol. 6354, 2010.

[18] C.Nwankpa, W.Ijomah, A.Gachagan and S.Marshall, "Activation Functions: Comparison of trends in Practice and Research for Deep Learning",arXiv : 1811.03378

[19] A.Krizhevsky, I.Sutskever and G.E.Hinton, "ImageNet classification with deep convolutional neural networks", Communications of the ACM, vol. 60, No. 6,pp 84–90

[20] J. Liu, Y.Pan, M. Li and Z.Chen, "Applications of deep learning to MRI images: A survey," Big Data Mining and Analytics, March 2018, vol. 1, no. 1, pp. 1-18

[21] G.Huang, Z.Liu, L. Maaten and K.Q.Weinberger, "Densely Connected Convolutional Networks",2018, arXiv:1608.06993 [cs.CV]

[22] S.Bringas, S Salomón , R. Duque, C. Lage and JL Montaña,"Alzheimer's Disease stage identification using deep learning models" J Biomed Inform., 2020 Sep;vol.. 109, 103514, Epub 2020 Jul 23

[23] S.Klöppel, CM. Stonnington, C.Chu, B.Draganski, RI. Scahill, JD. Rohrer, NC. Fox, CR. Jack, J.Ashburner and RSJ. Frackowiak, "Automatic classification of MR scans in Alzheimer's disease", Brain, vol. 131, Issue 3, pp. 681–689.

[24] Gray and K.Rachel: Machine learning for image-based classification of Alzheimer's disease. Ph.D. thesis, Imperial College London (2012)

[25] E. Hosseini-Asl, R.Keynton and A.El-Baz, "Alzheimer's disease diagnostics by adaptation of 3D convolutional network", 2016 Int. Conf. Image Process. (ICIP), 2016, pp. 126-130.

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