Diagnosing Alzheimer's Disease using Convolution Neural Networks

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Keywords: Alzheimer Disease, Convolution Neural Network, Deep Learning, Neurological Disorder

Introduction

A progressive neurodegenerative disease that induces nerve cell deaths and tissue loss in the brain is known as Alzheimer's Disease (AD), typically begins slower and grows worse with time (De la Torre and Stefano, 2000; Canter and Penney 2016). More than 5.5 million with age 65 years and above are affected by the AD (Alzheimer's, 2018) and become the leading cause of death among elder groups. The cost of managing, detecting and treating AD patients induces tremendous stress on every country's health care system (Schelke et al., 2018). The AD is a chronic, irreversible brain condition with deterioration in cognitive function (De Strooper and Karran, 2016). The detection of AD is focused on (a) lifespan prediction of patient, (b) possibilities of enhancing lifespan and (c) early detection of disease. Therefore, there has been much effort to develop early warning strategies, particularly during pre-symptomatic phases, to delay or prevent the disease's progression, as other two factors can be achieved by targeting the early detection of AD. The possibility to study in vitro pathological brain changes associated with AD is provided by Magnetic Resonance Imaging (MRI) (Veitch *et al.*, 2019). Neuro-imaging data have increasingly been used in the past decades to classify AD using Machine Learning (ML) techniques, which provide promising techniques to diagnose and prognosis of disease individually (Biswal *et al.*, 2010; Rathore *et al.*, 2017).

The diagnostic and detection of AD have improved significantly with the application of Machine Learning (ML) techniques such as Naive Bayes (NB), Support Vector Machine (SVM), Random Forest (RF), etc. (Zhang *et al.*, 2015; Arbabshirani *et al.*, 2017; Ludwig *et al.*, 2019). ML provides an intelligent system for developing an algorithm capable of analyzing the dataset variation, observing the pattern data and drawing valuable illustrations from the input data. Numerous experiments have been carried out using predefined features for the pre-processing of dataset integrating with a different algorithm to classify the dataset into binary or multiple classes (Farhan *et al.*, 2014; LeCun *et al.*, 2015; Samper-Gonzalez *et al.*, 2018). However, selection of appropriate



feature and classification is the complex and important steps in the detection of disease. Various statistical, probability, dynamic and stochastic models were used on the noisy, complex and non-linear dataset. Various machine learning and deep learning techniques shows tremendous growth in the accurate prediction for similar applications. The ML performs data analysis using four different steps involving extraction of appropriate features from the dataset, selecting specific features for further analysis, removing unnecessary information and classification of dataset following the identified feature. To perform these operations, detailed knowledge of the dataset and features that need to be extracted is the vital requirement before applying the ML techniques and training of model as well as segregation of dataset is a time-consuming task (Samper-Gonzalez et al., 2018). The selection of the appropriate feature extraction technique is the key to the ML algorithm's performance (LeCun et al., 2015; Samper-Gonzalez et al., 2018).

ML techniques limitations are effectively taken care of by the Deep Learning (DL) approaches, gaining popularity exponentially in the healthcare sector (Islam and Zhang, 2017; Razzak *et al.*, 2018). The DL techniques are the advanced version of ML techniques and can extract adequate features through representation-based learning methods (Krizhevsky *et al.*, 2012; Kushibar *et al.*, 2018).

The DL involves applying steps in sequential order following complex non-linear transformations in hierarchical order to identify the features and represent the data accordingly automatically. The application of multiple transformations in data helps extract the relevant information and remove the redundancy and dimensionality without the loss of relevant information. However, the complexities in dataset such as incompleteness, a smaller number of samples, large samples for only one or two class of dataset and sparseness induces difficulty in designing model and reduce the model performance.

The DL algorithms popularity in handling medical imagery and other object detection tasks has increased exceptionally due to the high accuracy and precision in model results (Jain et al., 2019). The application of DL techniques includes identification and diagnostics of medical images (Collobert et al., 2011), breast cancer detection (Liu et al., 2014), lung cancer detection (Hosseini-Asl et al., 2016), brain cell classification (Korolev et al., 2017) covers all the verticals of health care sectors. Among the various DL techniques, the Convolution Neural Network (CNN) is the generally used approach (Krizhevsky et al., 2012; Wen et al., 2018) for analysing neuroimaging images and prediction of the disease. The CNN is widely used over other deep leaning techniques such as LSTM, RNN, DNN and autoencoder-decoder. The CNN is capable of assigning similar weights to multiple neurons and vice versa to select the feature. The CNN algorithm was applied by various researchers for different applications and obtained high accuracy, although the sufficient number of samples sent for the model's training is the prime requirement of CNN along with the sufficient computation power and pre-processing of raw data. CNN effectively models the investigation of the multi-faceted essence of psychological and neurological diseases such as cross-modality interrelation like neuroimaging and genetics at the detailed level (Plis *et al.*, 2014).

In spite of availability of several techniques, a robust technique is required for the early prediction and classification of AD through variable dataset such as MRI scans either or two class or multiclass, in order to minimize the mortality rate and reduce the treatment cost by detecting the disease at the early stage. A methodology is formulated out to deal with the challenges of data augmentation. adequate size of sample set and drop out. DL techniques can be used efficiently to minimize the treatment cost by detecting the diseases at the early age by extracting the most relevant information from the images. The application of appropriate pre-processing techniques further resolves the problem. The MRI images observe several types of noises, distortions and artifacts while collecting the information, however, with the use of appropriate scaling method for resolving image resolution and registration, correction measures, trimming, normalization and filtering to improve the certain features of the image over spatial and temporal scale can improve the accuracy tremendously.

Literature Review

Deep learning approaches has been utilized to classify high-quality images into multiple classes, including computer vision (Krizhevsky *et al.*, 2012) and natural language processing (Collobert *et al.*, 2011), which are now showing extreme performance with high precision and accuracy. Several studies have been found using deep learning algorithm to handle the MRI images for the prediction and classification of disease. Identification of appropriate features extraction for the unbiased classification is the prime requirement. The process of training of model algorithm through sequence of steps are independent of earlier process (feature extraction), however, it affects the ultimate performance of the model, due to the interconnection between the techniques.

The CNN algorithm comes under the category of DL, which is further a subclass of machine learning and it is also the most popular algorithm mainly used in computer vision, language processing, image classification, face identification and more. CNN's capability to detect essential features from a given data with a spatial relationship without the need for human supervision and its highly efficient computation scheme makes it the best choice for image-related problems. The studies performed by various researchers in the classification of neuroimaging datasets and AD prediction using various deep learning architectures have been reviewed.

Use a support vector machine to diagnose AD patients. The dataset was collected from multiple scanners to technique's applicability identify the for the classification of mild AD patients from AD asymptomatic patients. However, the dimensional reduction and various other pre-processing techniques were applied by to investigate auxiliary MRI information. The author formed multiple classes to classify the AD from the MRI image using SVM classifiers. (Gupta et al., 2013) used a sparse autoencoder to study a set of bases from raw images and then involve convolution to extract features from the ADNI dataset and classify MRI cases into three categories: AD, MCI and Healthy Control (HC).

The extraction of multiple trained features from the each and every single image require the implementation of several ML techniques. (Liu et al., 2014) applied auto-encoder and softmax regression for generating the output of the mode in CNN to classify the neuroimaging dataset into multiple classes for the early detection of cancerous cells. The author contrasted the developed model's performance along with the conventional techniques and found that the proposed model requires less background information and less domain knowledge to design the model. Hosseini-Asl et al. (2016) designed a deep 3D CNN model for early detection of AD. The author applied the pre-trained transfer learning approaches to enhance the feature extraction efficiency and applied a deep CNN autoencoder algorithm for detailed classification of the AD dataset. Glozman and Liba (2016) also applied transfer learning techniques to train the database collected from ADNI using the ImageNet dataset and performed image pre-processing techniques to raise the sample set for model training.

Vieira *et al.* (2017) concluded that DL techniques provide a valuable tool for analyzing psychiatric and neurological disorders through neuro imagine images, for the assessment and division of brain disease, for the extraction of desired features from neuro imagine images. The comparison of various techniques on similar dataset reveals significant information about the data, which may not be identified by single technique for the classification of images in binary or multiclass. Jo *et al.* (2019) compared and reviewed the various studies performed on the classification of AD and concluded that the model's performance could be enhanced by producing the ensembled approach of DL techniques with biomarkers. However, the large size of the dataset requires greater computational power and adequate training time to obtain higher accuracy.

El-Sappagh *et al.* (2020) proposed the multimodel hybrid network of CNN and Bi-LSTM to predict the multiple parameters through time-series data. The most relevant features were extracted using ANN and the hybrid technique was used for the classification and regression. Abuhmed *et al.* (2021) developed multiple architectures using Bi-LSTM. The one architecture is designed along with the regression to predict the most significant feature and another architecture is designed for the classification using the ADNI dataset. The models are evaluated using multiple evaluation measures that resulted in 80.3% accuracy, 80.8% recall, 81.65% precision and 81.19% F1 score. Noor et al. (2020) compared the techniques for the analysis of multiple neurological disorders, including AD Schizophrenia (SZ) and Parkinson's Disease (PD), using MRI images. The author observed that CNN have been used dominantly to detect AD and PD, whereas DNN is the first choice of researchers for the detection of SZ. Various open-source datasets are available for the prediction and classification of various brain diseases. Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset consist of MRI neuroimaging dataset of normal and AD class. ADNI dataset further composed of ADNI-1, ADNI-2, ADNI-3 and ADNI-GO consisting data of various categories of disease (Weiner, 2004). Open access series of imaging studies known as (OASIS dataset) is also open-source data consisting longitudinal neuroimaging and biomarkers data for AD (OASIS, 2007). Other than these datasets, MIRIAD (UCL, 2020), COBRE (Network, 2012) and FBIRN (Keator et al., 2015) are also commonly used datasets for the classification of AD classes.

The comparison of various techniques for the evaluation of best features extraction technique indicates that, there are certain limitations of techniques that causes the low accuracy in the classification of normal images from AD (Sabuncu and Konukoglu, 2015). The noises and distraction in the MRI images are the major hindrances that cause the low accuracy and make the model biased towards the larger sample set and lead to the inaccurate results. The voxel feature induces lot of noise in the MRI images and require the implementation of smoothing and clustering techniques to reduce the biasness and improve the prediction accuracy (Dauphin et al., 2012). The pre-processing techniques used in the model before the classification, greatly influence the extraction of feature vector. However, the models use trained features are dependent upon the multi-class dataset and also found producing biased results towards a particular class having large number of samples in comparison to the other. The developed classification model accuracy significantly depends upon features vectors available in the dataset and pre-processing techniques applied for the extraction of feature vector used in the training of the model as well as the application of domain knowledge.

The study was performed to detect AD and classify the disease on the bases of MRI data using CNN. The proposed network is specifically designed for the small dataset to identify the model's performance in the diagnostics of AD and to state a reliable approach to master a deep learning prototype within the computational constraints. The DL techniques can withstand the complex dataset containing multiple features by extracting the adequate features to perform the classification. The CNN is applied over the multiple layers of features by training the model to extract the relevant information on observing the new samples of dataset.

Materials and Methodology

Database

The Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset (Long *et al.*, 2017) was collected in the NIFTI (.nii) format. With a view to read the image data, a nibabel python package is used. ADNI dataset consist of pre-processed images with biomarkers which reduces the computational time drastically had preferred over other datasets. Data is loaded into the memory using the load function of the nibabel package. Once loaded, data is available in the form of NumPy arrays. Since the ADNI images are 3D images of the brain, the NumPy array is of three dimensions. Images can be plotted, one axis at a time, using the matplotlib python package.

Each axis plots all the rest of the two axes' pixels and only one instance of the selected axis, which is Fig. 1. Reading the data using the load () function of the nibabel package takes care of the image's affine transformations. There are multiple MRI machines used to capture image data in ADNI Project. As a result, there are multiple dimensions of the input images, depending upon which machine was used to capture the MRI image. All input images are resized such that the output images after resizing all have the same dimensions. The output dimensions of all the images are selected to be 160 x 160 x 128 after resizing the images, Fig. 2.

ADNI contains the normalized and unwarped images. All the images are gone through specific pre-processing techniques to provide several corrections. Grad warp is performed to provide to avoid the distortion in the image due to non-linearity. The B1 is applied to produce` the uniformity in the images. The N3 is applied to provide sharpening of the images and all three pre-processing techniques are applied in a sequence to avoid loss of any information. ADNI scientists gather, approve and use information, including MRI images, PET images, hereditary qualities, subjective tests, CSF, blood biomarkers, etc. as indicators of the ailment (Long *et al.*, 2017).

The subjects were put under categorization into groups of NC and AD patients. The dataset contains the large number of images; however, only selective images contain the relevant information and can be used successfully for the detection of disease. The desired information is very minute and precise extraction is required. The required feature extraction from the dataset for the training of the model with an objective to classify the images containing features reflecting disease information from the normal images.

This research deals with the detection of Alzheimer's disease using the CNN algorithm for medical applications from MRI images. CNN can be trained efficiently by using only a small data set and these are the factors that give our system good performance and accuracy in the diagnosis of AD. Every input image pixel is mapped by recording the relevant information from different features and clubbed to generate the model output.

Convolution Neural Network Framework

A straight forward ConvNet is the layer grouping method and every layer of a ConvNet tends to change one volume of activation to another by a differentiable capacity. We used three principal layers to build ConvNet structures: Convolutional Layers, Pooling Layer and Fully-Connected Layer and these particular layers are allocated accordingly to shape a full ConvNet design. The multiple iterations of model are performed to obtain the final architecture of CNN model so as to get the model with highest accuracy. The initial layet perform the classification using unsupervised features, whereas the classifier helps to identify the features through fully connected layers, which in turn assist in the fine-tuning of selected features and also improves the model performance.

The number of instances of each layer is identified through multiple iterations to locate the features. The precise sequence of multiple convolution and Fully-Connected (FC) layers are identified to connect with pooling layer. The ReLU activation function (Rectified Linear Unit) is applied in the model followed by softmax pooling layer to reduce the output layer. The model architecture which was utilized for this work is INPUT-CONV-RELU- POOL-FC. 3D Input [160x160x128] will carry the raw pixel estimations of the image.

The multiple convolutions and fully connected layer are required to extract the exact information from the images. As the single image or section of the images cannot extract all the relevant information, multiple layers are used. All the convolution layer are super imposed to get the maximum information at each pixel in the model training. Additional number of layers helps in the handling the complex data containing large number of features at different instances. At the last stage, softmax function is used to reduce the fully connected layer to single output, which is also used for the representation of image whether it falls into AD or normal category.

Convolution Layer

The convolution layer forms the CNN and the basic structure involves the neurons with different weights and biases located within multiple fully interconnected layers (Lecun *et al.*, 1998). The convolution layer is the main component of the entire framework, which holds extensive data. The convolution layer selects the kernel k, stride s, padding p and image size $m \ge n$ and applies the operations to generate the output (Lecun *et al.*, 1998):

$$Output \ size = \frac{m-k+2p}{s+1} X \frac{n-k+2p}{s+1}$$

The type and number of kernels operate to select the neuron's appropriate feature and field to maintain the connectivity with the other neurons of previous layers. The output O obtained from the matrix A having size of (P, Q) and matrix B having a size of (X, Y) after

performing the operations (Goodfellow *et al.*, 2016) in the convolution layer is explained mathematically as:

$$O(i,j) = \sum_{P=0}^{P-1} \sum_{Q=0}^{Q-1} A(P,Q) * B(i-P,j-Q)$$

where, $1 - X \le i \le P-1$ and $1-Y \le j \le Q-1$.

The summation of all the matrix product is performed for each neuron. For example, at O(0, 0), the matrix B is rotated at 1800 and multiplied with the matrix A. However, the rotation of element can be avoided in the convolution layer and the output in convolution would express as:

$$O(i,j) = \sum_{P=0}^{p-1} \sum_{Q=0}^{Q-1} A(P,Q)^* B(P-i,Q-j)$$

where, $1 - X \le i \le P - 1$ and $1 - Y \le j \le Q - 1$.

Pooling Layer

The nodes in the convolution and pooling layers are accountable for CNN's automated feature selection ability. The pooling operation extracts the maximum size of the image of $m \ge n$ size. Pooling layer output is expressed as:

$$Output size = \frac{m-k}{s+1} X \frac{w-k}{s+1}$$

The pooling layer's primary function is to minimize unnecessary information by decreasing the dimension of the input data without the loss of any vital data or information. This, in turn, reduces the computational efforts required for the model training. The problems associated with the overfitting and under fitting can also be resolved by applying the pooling operations.

Activation Function

The convolutional layers are derived by both the linear and non-linear layers containing activation functions like Rectified Linear Unit (ReLU) and sigmoid. The ReLU has overcome the disadvantages of sigmoidal and tanh activation function and most commonly used for deep learning operations. The multiple variants of Re LU are adopted in deep learning (Nair and Hinton, 2010), which is expressed as:

$$f(x) = \max(0, x) ReLU$$
 function

$$f(x) = \begin{cases} x, x > 0\\ 0.01x, otherwise \end{cases}$$
 Leaky ReLU function:

$$f(x) = \begin{cases} x, x > 0\\ a(e^x - 1), otherwise, where a \ge 0 \end{cases}$$

Exponential ReLU function

The network displays a single separable function throughout the network layers from input raw image pixels to the final layer with softmax activation function at the final layer (Bringas *et al.*, 2019).



Fig. 1: (a) The plot of second and third axes pixels; (b) Plot of first and third axes pixels; (c) Plot of first and second axes pixels of Brain MRI Image



Fig. 2: The sagittal view of MRI from NC to the development of AD (from left to right)



Fig. 3: The architecture of CNN containing input, convolution, pooling, fully connected and output layer (Bringas *et al.*, 2019)

Fully Connected Layer

All the neurons in this layer are fully connected to the activation function of CNN. The neurons in CNN are arranged in a three-dimensional structure as per the height, width and depth of the input data set, which is not found in general neural network schemes. The classification is performed after attaching fully connected layers with the other layers (convolution and pooling). Figure 3 shows the detailed architecture of CNN used to binary classification of Alzheimer's disease.

Results and Discussion

Experimental Setup

AD escalates commonly in old age and causes the degradation of few brain cells. The AD symptoms are dominantly observed after 65 years and the sample set is identified accordingly. The Keras library written in Tensor flow is used for designing the classification model in Python 3.8. The batch size of 32 is designed for the training of the model and iterated for 50 epochs. Each epoch passed through multiple steps in the forward and backward direction of the network. The dataset is divided into three subsets, 70% for the training, 15% for testing and the rest for the validation and the model is validated based on the performance of training and testing results. The 3-D convolutional layer has a size of $5 \times 5 \times 5$ units with strides 1 and 'SAME' padding such that the shape of the output is equivalent to the input tensor. The max pool layer has kernel size of $4 \times 4 \times 4$ and stride of $4 \times 4 \times 4$ with padding = 'SAME' so that dimensions of output tensor is equal to input tensor. The first fully connect layer has 1024 neurons deeply connected with second fully connected layer having 2 neurons, which is equivalent to the number of output classes. Default learning rate of Adam's optimizer is used in the study, i.e., 0.001. The softmax is used as a classifier to improve the training time. The pooled features are entered in the feed-forward back propagation based neural network models. The exact number of hidden layers are identified after several iteration and validation accuracy results.

Data Classification

The performance of the developed classification model is estimated based on several measures, including accuracy, precision, recall, confusion matrix and F1-score. Among all the evaluation measures, the confusion matrix's design is the critical measure that helps in the assessment of the applicability of the model in four combinations derived from the positive and negative prediction of actual and predicted results. The value of the confusion matrix is used to determine the accuracy, precision and recall. Table 1 contains the results of a confusion matrix.

The data in the Table 1 are read in the matrix form and denoted TP, FP, TN and FN as the true positive, false positive, true negative and false negative. In between the actual and predicted AD, 58 represents the True Positive (TP), representing the correct number of samples determined by the model and 11 represents the False Positive (FP), which represents an incorrect number of the sample identified as the correct samples by the model. Whereas 8 represent the False Negative (FN), representing a correct number of the sample determined by the incorrect samples and 73 represent the True Negative (TN), which is the incorrect number of the model detected by the model incorrect samples.

The confusion matrix results are utilized to determine the other evaluation parameters, including accuracy, precision, recall and F1-score. The evaluation parameters are determined using the following expressions:

$$Accuarcy = \frac{TP + TN}{TP + FP + FN + TN}$$
$$Precision = \frac{TP}{TP + FP}$$
$$Re call = \frac{TP}{TP + FN}$$
$$F1Score = 2*\frac{Precision * Recall}{Precision + Recall}$$

The accuracy referred to the proportion of correct predictions and derived from the binary classification of Alzheimer patients from the total dataset and the rest of the samples is considered normal. The accuracy is the very first parameter always considered as the measure for the evaluation of developed model, as it provides the percentage of correct prediction from the total dataset. An accuracy of 87.3% was obtained from the classification model. The training loss were measured and found low at 15th epoch and concise to the minimum value at the 39th epoch. The accuracy results are obtained on the trained model and indicates that model would be able to generate the accuracy of 87.3% for further predictions of classification for similar images. The other evaluation measures are also necessary to ensure the adequacy of the proposed model. Only accuracy may sometime induce incorrect assessment of the results due to the biased other classification, however, the values of performance evaluation measures indicate the adequacy of the proposed model. If the values of the evaluation measures are falling in the approximately close to each other, that reflects that model is unbiased for the specific set of images irrespective of difference in number of images for a particular class. The precision of any model is determined based on the correctly predicted positive observation ratio compared to the total positive samples. The precision obtained in the model was 84.05%. The recall indicates the ratio of true positives responses from the actual samples against the sum of both the true positives and incorrectly predicted responses as the correct responses. If the model predicts many samples as a correct response, those samples are incorrect and hold the negative response; the models are not acceptable for the prediction. The recall obtained in the study was 87.87%. The Table 2 depicts the performance of proposed model contrary to the various evaluation measures.

The sensitivity is the sum of both the precision and recall, whereas twice the ratio of two to the sum of two represents the F1 Score. The F1 Score is computed based on precision and recall scores, determined as the weighted avg of precision and recall scores. The most appropriate value of the F1 Score is determined if the model has a balanced value of precision and recall. However, the significant difference in precision and recall values produces the lower value of the F1 Score. The F1 Score observed in the model was 85.91%. The variation inaccuracy is also observed to identify the appropriate batch size. Results show that the highest rise in accuracy is acquired at the iterative model of 40 epochs. The epoch consider in the model are equivalent to the no change in accuracy up to three decimal places. The CNN technique provides the output with the extraction of both the highly significant and discrete features which results in high accuracy and better performance of proposed model in all the performance evaluation measures. The strong feature extraction technique and application of trained features assist in handling complex dataset.

The comparison of the proposed model is also carried out with the studies available in literature as shown in Table 3. The accuracy obtained from the proposed model comes out to be 87.3%, which is an apparent rise in accuracy compared to the previous studies performed for a similar type of data and utilizing a similar technique, clearly reveals the effectiveness of the proposed model. As compared to the previous models, the proposed model is capable of image classification using Adam optimization algorithm, which allows the model to capture each patch individually and multiple times through different layers. The algorithm allows the model to record every minute information, as the brain cell features are very subtle in nature and iterative process is required to extract the relevant information. Figure 4 shows comparison of results of proposed model with previously carried out studies. The multiinstance learning in the proposed model through multiple layers allows the capturing of every subtle information and increase the accuracy in comparison to previously studied models. The model generates the promising results that can be used with the larger dataset also and validate the strength of the model.

Table 1: Confusion matrix for CNN classification model

		Actual	
•		AD	NC
Predicted	AD	58	8
	NC	11	73

Table 2: AD vs. NC cl	assification performance of	proposed model			
Model	Classification	Accuracy	Precision	Recall	F1-Score
Proposed Model	AD vs. NC	0.87	0.84	0.88	0.86
Table 3: Comparison of	of the proposed model with a	available models			
Model		Classification			Accuracy
		AD vs. NC			80.0
Glozman and Liba (2016)		AD vs. NC			83.57
Proposed model		AD vs. NC			87.3
^					



Fig. 4: Comparison of proposed model with the models available in literature

Conclusion

In recent times, convolutional neural networks applications have increased exceptionally and have been extensively used to extract information from images, analyze and classify the data. The CNN models have also performed exceptionally in the broad area of application. The CNN architecture makes it assist in the classification of AD patients with respect to other normal cases by recognizing the information from each pixel and learning the input dataset in the set of small groups. This study exhibits an automated AD diagnosis and a classification framework for the timely treatment of the patients. The proposed frameworks take the MRI image of a patient's brain and then apply a convolutional pooling layer to segregate the features and based on this, it classifies the image as either AD or NC. The performance of the CNN model is evaluated through the confusion matrix, accuracy, precision and recall and F1 Score. The developed model is also compared with other previously available studies carried by researchers on the similar technique. The proposed model can extract the vital information and delivers an accuracy of 87.3%.

efficient in terms of accuracy on selected dataset and there is no requirement to perform any supervised feature extraction and be capable of dealing with both the large and small medical image datasets. The proposed method excels in better accuracy compared to other methods. Compared with the previous models, the proposed model is capable to classify the images using Adam optimization algorithm, which allows the model to capture each patch individually and multiple times through different layers. For further studies, the model can be coupled with another state the art approaches to design the more rigid

The method used in proposed work is good and

another state the art approaches to design the more rigid classifier. The application of pre-processing approaches to enhance image features could also be tested to identify the variation in model performance. Pre-trained models with transfer learning can be explored for this problem in the future for a better result on a large dataset. However, in the proposed model there is scope of some improvements also. The upgraded model could be trained for the multi class classification and prediction of disease. Other than Alzheimer, Parkinson Disease (PD) (Pereira *et al.*, 2020) and Schizophrenia (Qiu *et al.*, 2019) are the other commonly observed neurological disorders and model can be trained and validated for the classification of other disease also. (Noor *et al.*, 2020) also reveals that CNN is the model efficient and robust technique for the early prediction and classification of AD, PD and other neurological disorders and study could be further enhanced to identify the other diseases. The proposed model works in two stages, first stage take care of training of features and second stage is the classification of images. However, the feature training and classification can be clubbed in future studies.

In continuation of this study, it is proposed to further work on the development of model for the classification of multi class data and simulation for early disease detection. The multi-class problem would raise the challenges such as complexity of dataset, implementation of multiple pre-processing techniques and selection of appropriate features for classification. However, it is proposed to test the model on the various dataset like ADNI-1, ADNI-2, ADNI-3, ADNI-GO, MIRIAD, COBRE and FBIRN (Keator *et al.*, 2015).

Author's Contributions

Sarita: Participated in all experiments, coordinated the analysis and contributed to the writing of the manuscript.

Saurabh Mukherjee: Guided the whole manuscript and help to find the material and methods.

Tanupriya Choudhury: Guided the whole manuscript and completed the survey and wrote the conclusion and reff and wrote the discussions part.

Kush Kulshrestha: Helped for data analysis and generated the methods in experimental conditions.

Ruby Singh: Helped and formulated the review responses, designed the figures and formulated the results.

Ethics

The article is original and contains unpublished materials. The all authors have read and approved the manuscript and no ethical issues are involved and there is no conflict of interest in between authors.

References

- Abuhmed, T., El-Sappagh, S., & Alonso, J. M. (2021). Robust hybrid deep learning models for Alzheimer's progression detection. Knowledge-Based Systems, 213, 106688. doi.org/10.1016/j.knosys.2020.106688
- Alzheimer's, A. (2018). 2018 Alzheimer's disease facts and figures. Alzheimer's & Dementia, 14(3), 367-429. doi.org/10.1016/j.jalz.2018.02.001
- Arbabshirani, M. R., Plis, S., Sui, J., & Calhoun, V. D. (2017). Single subject prediction of brain disorders in neuroimaging: Promises and pitfalls. Neuroimage, 145, 137-165.

- Biswal, B. B., Mennes, M., Zuo, X. N., Gohel, S., Kelly, C., Smith, S. M., ... & Milham, M. P. (2010). Toward discovery science of human brain function. Proceedings of the National Academy of Sciences, 107(10), 4734-4739. doi.org/10.1073/pnas.0911855107
- Bringas, S., Salomón, S., Duque, R., Montaña, J. L., & Lage, C. (2019). A Convolutional Neural Network-Based Method for Human Movement Patterns Classification in Alzheimer's Disease. In Multidisciplinary Digital Publishing Institute Proceedings (Vol. 31, No. 1, p. 72). doi.org/10.3390/proceedings2019031072
- Canter, R. G., Penney, J., & Tsai, L. H. (2016). The road to restoring neural circuits for the treatment of Alzheimer's disease. Nature, 539(7628), 187-196. doi.org/10.1038/nature20412
- Collobert, R., Weston, J., Bottou, L., Karlen, M., Kavukcuoglu, K., & Kuksa, P. (2011). Natural language processing (almost) from scratch. Journal of machine learning research, 12(ARTICLE), 2493-2537.
- Dauphin, G. M. Y., Glorot, X., Rifai, S., Bengio, Y., Goodfellow, I., Lavoie, E., ... & Bergstra, J. (2012, June). Unsupervised and transfer learning challenge: A deep learning approach. In Proceedings of ICML Workshop on Unsupervised and Transfer Learning (pp. 97-110). JMLR Workshop and Conference Proceedings. http://proceedings.mlr.press/v27/mesnil12a.html
- De la Torre, J. C., & Stefano, G. B. (2000). Evidence that Alzheimer's disease is a microvascular disorder: The role of constitutive nitric oxide. Brain research reviews, 34(3), 119-136. doi.org/10.1016/S0165-0173 (00)00043-6
- De Strooper, B., & Karran, E. (2016). The cellular phase of Alzheimer's disease. Cell, 164(4), 603-615. doi.org/10.1016/j.cell.2015.12.056
- El-Sappagh, S., Abuhmed, T., Islam, S. R., & Kwak, K. S. (2020). Multimodal multitask deep learning model for Alzheimer's disease progression detection based on time series data. Neurocomputing, 412, 197-215. doi.org/10.1016/j.neucom.2020.05.087
- Farhan, S., Fahiem, M. A., & Tauseef, H. (2014). An ensemble-of-classifiers based approach for early diagnosis of Alzheimer's disease: Classification using structural features of brain images. Computational and mathematical methods in medicine, 2014.
- Glozman, T., & Liba, O. (2016). Hidden Cues: Deep Learning for Alzheimer's Disease Classification. CS331B project final report, 1-8. https://scholar.google.com/scholar?cites=106267086 65182760584&as_sdt=2005&sciodt=0,5&hl=en
- Goodfellow, I., Bengio, Y., & Courville, A. (2016). Deep learning. MIT press.
- Gupta, A., Ayhan, M., & Maida, A. (2013, May). Natural image bases to represent neuroimaging data. In International conference on machine learning (pp. 987-994). PMLR. http://proceedings.mlr.press/v28/gupta13b.html

- Hosseini-Asl, E., Gimel'farb, G., & El-Baz, A. (2016). Alzheimer's disease diagnostics by a deeply supervised adaptable 3D convolutional network. arXiv preprint arXiv:1607.00556. https://arxiv.org/abs/1607.00556
- Islam, J., & Zhang, Y. (2017, November). A novel deep learning based multi-class classification method for Alzheimer's disease detection using brain MRI data. In International Conference on Brain Informatics (pp. 213-222). Springer, Cham.
- Jain, R., Jain, N., Aggarwal, A., & Hemanth, D. J. (2019). Convolutional neural network based Alzheimer's disease classification from magnetic resonance brain images. Cognitive Systems Research, 57, 147-159. doi.org/10.1016/j.cogsys.2018.12.015
- Jo, T., Nho, K., & Saykin, A. J. (2019). Deep Learning in Alzheimer's Disease: Diagnostic Classification and Prognostic Prediction Using Neuroimaging Data. Frontiers in Aging Neuroscience, 11. doi.org/10.3389/fnagi.2019.00220
- Keator, D. B. (2015) The function biomedical informatics research network data repository. NeuroImage. doi.org/10.1016/j.neuroimage .2015.09.003
- Korolev, S., Safiullin, A., Belyaev, M., & Dodonova, Y. (2017, April). Residual and plain convolutional neural networks for 3D brain MRI classification. In 2017 IEEE 14th international symposium on biomedical imaging (ISBI 2017) (pp. 835-838). IEEE. doi.org/10.1109/ISBI.2017.7950647
- Krizhevsky, A., Sutskever, I., & Hinton, G. E. (2012). Imagenet classification with deep convolutional neural networks. In Advances in neural information processing systems (pp. 1097-1105).
- Kushibar, K., Valverde, S., González-Villà, S., Bernal, J., Cabezas, M., Oliver, A., & Lladó, X. (2018). Biswal, B.
 B., Mennes, M., Zuo, X. N., Gohel, S., Kelly, C., Smith, S. M., ... & Milham, M. P. (2010). Toward discovery science of human brain function. Proceedings of the National Academy of Sciences, 107(10), 4734-4739. doi.org/10.1073/pnas.0911855107
- LeCun, Y., Bengio, Y., & Hinton, G. (2015). Deep learning. nature, 521(7553), 436-444.
- LeCun, Y., Bottou, L., Bengio, Y., & Haffner, P. (1998). Gradient-based learning applied to document recognition. Proceedings of the IEEE, 86(11), 2278-2324. doi.org/10.1109/5.726791
- Liu, S., Liu, S., Cai, W., Pujol, S., Kikinis, R., & Feng, D. (2014). Early diagnosis of Alzheimer's disease with deep learning. 2014 IEEE 11th International Symposium on Biomedical Imaging (ISBI). doi.org/10.1109/isbi.2014.6868045
- Long, X., Chen, L., Jiang, C., Zhang, L., & Alzheimer's Disease Neuroimaging Initiative. (2017). Prediction and classification of Alzheimer disease based on quantification of MRI deformation. PloS one, 12(3), e0173372. doi.org/10.1371/journal.pone.0173372

- Ludwig, N., Fehlmann, T., Kern, F., Gogol, M., Maetzler, W., Deutscher, S., ... & Metzger, F. (2019). Machine learning to detect Alzheimer's disease from circulating non-coding RNAs. Genomics, proteomics & bioinformatics, 17(4), 430-440.
- Nair, V., & Hinton, G. E. (2010, January). Rectified linear units improve restricted boltzmann machines. In Icml. https://openreview.net/forum?id=rkb15iZdZB
- Network, T. M. R. (2012) COBRE MR data. https ://bit.ly/2Qdrj sd Accessed 2020-12-26
- Noor, M. B. T., Zenia, N. Z., Kaiser, M. S., Al Mamun, S., & Mahmud, M. (2020). Application of deep learning in detecting neurological disorders from magnetic resonance images: A survey on the detection of Alzheimer's disease, Parkinson's disease and schizophrenia. Brain informatics, 7(1), 1-21. doi.org/10.1186/s40708-018-0080-3
- OASIS: OASIS Brains Dataset (2007). https://www.oasis -brain s.org/Accessed 2020-12-26
- Pereira, H. R., Fonseca, J. M., & Ferreira, H. A. (2020, April). Combination of Medical Imaging and Demographic Data for Parkinson's Disease Diagnosis. In DoCEIS (pp. 339-346).
- Plis, S. M., Hjelm, D. R., Salakhutdinov, R., Allen, E. A., Bockholt, H. J., Long, J. D., ... & Calhoun, V. D. (2014). Deep learning for neuroimaging: A validation study. Frontiers in neuroscience, 8, 229. doi.org/10.3389/fnins.2014.00229
- Qiu, Y., Lin, Q. H., Kuang, L. D., Zhao, W. D., Gong, X. F., Cong, F., & Calhoun, V. D. (2019, July). Classification of schizophrenia patients and healthy controls using ICA of complex-valued fMRI data and convolutional neural networks. In International Symposium on Neural Networks (pp. 540-547). Springer, Cham. doi.org/10.1007/978-3-030-00931-1_34
- Rathore, S., Habes, M., Iftikhar, M. A., Shacklett, A., & Davatzikos, C. (2017). A review on neuroimaging-based classification studies and associated feature extraction methods for Alzheimer's disease and its prodromal stages. NeuroImage, 155, 530-548. doi.org/10.1016/j.neuroimage.2017.03.057. Epub 2017 Apr 13. PMID: 28414186; PMCID: PMC5511557
- Razzak, M. I., Naz, S., & Zaib, A. (2018). Deep learning for medical image processing: Overview, challenges and the future. In Classification in BioApps (pp. 323-350). Springer, Cham.
- Sabuncu, M. R., Konukoglu, E., & Alzheimer's Disease Neuroimaging Initiative. (2015). Clinical prediction from structural brain MRI scans: A large-scale empirical study. Neuroinformatics, 13(1), 31-46. doi.org/10.1007/s12021-014-9238-1

- Samper-Gonzalez, J., Burgos, N., Bottani, S., Fontanella, S., Lu, P., Marcoux, A., ... & Bertrand, A. (2018). Reproducible evaluation of classification methods in Alzheimer's disease: Framework and application to MRI and PET data. NeuroImage, 183, 504-521.
- Schelke, M. W., Attia, P., Palenchar, D. J., Kaplan, B., Mureb, M., Ganzer, C. A., ... & Isaacson, R. S. (2018). Mechanisms of risk reduction in the clinical practice of Alzheimer's disease prevention. Frontiers in aging neuroscience, 10, 96. doi.org/10.3389/fnagi.2018.00096
- UCL. (2020) Minimal Interval Resonance Imaging in Alzheimer's Disease (MIRIAD). Last Accessed on 2020-12-12. http://miria.d.drc.ion.ucl.ac.uk/
- Veitch, D. P., Weiner, M. W., Aisen, P. S., Beckett, L. A., Cairns, N. J., Green, R. C., ... & Alzheimer's Disease Neuroimaging Initiative. (2019). Understanding disease progression and improving Alzheimer's disease clinical trials: Recent highlights from the Alzheimer's Disease Neuroimaging Initiative. Alzheimer's & Dementia, 15(1), 106-152. doi.org/10.1016/j.jalz.2018.08.005

- Vieira, S., Pinaya, W. H., & Mechelli, A. (2017). Using deep learning to investigate the neuroimaging correlates of psychiatric and neurological disorders: Methods and applications. Neuroscience & Biobehavioral Reviews, 74, 58-75. doi.org/10.1016/j.neubiorev.2017.01.002
- Weiner, M. W. (2004) Alzheimer's Disease Neuroimaging Initiative. http://adni.loni.usc.edu/ Accessed 2019-12-26
- Wen, D., Wei, Z., Zhou, Y., Li, G., Zhang, X., & Han, W. (2018). Deep learning methods to process fmri data and their application in the diagnosis of cognitive impairment: A brief overview and our opinion. Frontiers in neuroinformatics, 12, 23. doi.org/10.3389/fninf.2018.00023
- Zhang, Y., Dong, Z., Phillips, P., Wang, S., Ji, G., Yang, J., & Yuan, T. F. (2015). Detection of subjects and brain regions related to Alzheimer's disease using 3D MRI scans based on eigenbrain and machine learning. Frontiers in computational neuroscience, 9, 66.