Chapter-01: INTRODUCTION

1.1 General Introduction

Alzheimer's disease (AD) is a complex neurological disorder with economic, social, and medical burdens which is acknowledged as leading cause of dementia marked by the accumulation and aggregation of amyloid-β peptide and phosphorylated tau (p-tau) protein and concomitant dementia, neuron loss and brain atrophy. AD is the most prevalent neurodegenerative brain disorder with sporadic etiology, except for a small fraction of cases with familial inheritance where familial forms of AD are correlated to mutations in three functionally related genes: the amyloid-β protein precursor and presenilin's 1 and 2, two key γ-secretase components. The common clinical features of AD are memory impairment that interrupts daily life, difficulty in accomplishing usual tasks, confusion with time or place, trouble understanding visual images and spatial relationships. Age is the most significant risk factor for AD, whereas other risk factors correlated with AD are hypercholesterolemia, hypertension, atherosclerosis, coronary heart disease, smoking, obesity, and diabetes. Despite decades of research, there is no satisfying therapy which will terminate the advancement of AD by acting on the origin of the disease process, whereas currently available therapeutics only provide symptomatic relief but fail to attain a definite cure and prevention. This review also represents the current status of AD in Bangladesh.

Several statistical and machine learning models have been exploited by researchers for Alzheimer's disease diagnosis. Recently, advanced deep learning techniques and image processing have successfully demonstrated human-level performance in numerous fields including medical image analysis. We propose a deep convolutional neural network for Alzheimer's disease diagnosis using brain MRI data analysis. While most of the existing approaches perform binary classification, our model can identify different stages of Alzheimer's disease and obtains superior performance for early-stage diagnosis. [2]

1.2 Objective

Alzheimer's disease destroys brain cells causing people to lose their memory, mental functions and ability to continue daily activities. It is very hard to detect at the early stages. The objective to build a model that will detect the AD from brain MRI images at the early stages. So that the patient gets proper treatment. The objective of feature selection is to select discriminate features with low relevance between each other and high relevance to the outcome. The degenerated brain cells have low intensity in MRI images. For accurate disease diagnosis, researchers have developed several computer-aided diagnostic systems.

1.3 Alzheimer's Symptoms

Remember Alzheimer's affects everyone differently. The timing and severity may be different for each person and it can be difficult to determine which stage our loved one is in because stages may overlap and are only meant to be a guideline. [1] There are some symptoms of Alzheimer's disease:

Stage 1: Noticeable Memory Difficulties

- Have trouble remembering recently read material, such as books or magazines
- Find remember plans and organizing increasing difficult
- Have more difficulty retrieving a name or word
- Experience challenges in social settings or work

Stage 2: More than Memory Loss

- Confusion about what day it is and where they are
- Increased risk of wandering off or getting lost
- Changes in sleep patterns, such as restlessness at night and sleeping during the day
- Difficulty choosing appropriate clothing for the weather or the occasion

Stage 3: Decreased Independence

Emotional changes are also common during this stage, including:

- Hallucinations: Seeing things that aren't there
- Delusions: False beliefs that you believe to be true
- Paranoia: The feeling that others are against you

Stage 4: Lack of Physical Control

Alzheimer's destroys brain cells, and eventually, this can cause severe mental and physical impairment. Our loved one's body may begin to shut down as their mind struggles to communicate and delegate tasks effectively.

At this point, our loved one's need will significantly increase. They may need round-the-clock care for help with walking, sitting and eventually swallowing.

Because of their reduced mobility, their body can also become vulnerable to infections, such as pneumonia. To help avoid infections, keep their teeth and mouth clean, treat cuts and scrapes with an antibiotic ointment right away, and make sure they get their flu shot each year.

1.4 Causes of Alzheimer’s

The exact causes of Alzheimer's disease aren't fully understood. But at a basic level, brain proteins fail to function normally, which disrupts the work of brain cells (neurons) and triggers a series of toxic events. Neurons are damaged, lose connections to each other and eventually die.

Scientists believe that for most people, Alzheimer's disease is caused by a combination of genetic, lifestyle and environmental factors that affect the brain over time.

Less than 1% of the time, Alzheimer's is caused by specific genetic changes that virtually guarantee a person will develop the disease. These rare occurrences usually result in disease onset in middle age.

The damage most often starts in the region of the brain that controls memory, but the process begins years before the first symptoms. The loss of neurons spreads in a somewhat predictable pattern to other regions of the brains. By the late stage of the disease, the brain has shrunk significantly.

1.5 Risk Factor

1. **Age**

Increasing age is the greatest known risk factor for Alzheimer's disease. Alzheimer's is not a part of normal aging, but as you grow older the likelihood of developing Alzheimer's disease increases.

2. **Family history and genetics**

Your risk of developing Alzheimer's is somewhat higher if a first-degree relative — your parent or sibling — has the disease. Most genetic mechanisms of Alzheimer's among families remain largely unexplained, and the genetic factors are likely complex.

3. **Down syndrome**

Many people with Down syndrome develop Alzheimer's disease. This is likely related to having three copies of chromosome 21 — and subsequently three copies of the gene for the protein that leads to the creation of beta-amyloid. Signs and symptoms of Alzheimer's tend to appear 10 to 20 years earlier in people with Down syndrome than they do for the general population.

4. **Sex**

There appears to be little difference in risk between men and women, but, overall, there are more women with the disease because they generally live longer than men.

5. Mild cognitive impairment

Mild cognitive impairment (MCI) is a decline in memory or other thinking skills that is greater than normal for a person's age, but the decline doesn't prevent a person from functioning in social or work environments.

6. Excessive alcohol consumption

Drinking large amounts of alcohol has long been known to cause brain changes. Several large studies and reviews found that alcohol use disorders were linked to an increased risk of dementia, particularly early-onset dementia.

7. Poor sleep patterns

Research has shown that poor sleep patterns, such as difficulty falling asleep or staying asleep, are associated with an increased risk of Alzheimer's disease.

8. Lifestyle and heart health

Research has shown that the same risk factors associated with heart disease may also increase the risk of Alzheimer's disease. These include:

- Lack of exercise
- Obesity
- Smoking or exposure to secondhand smoke
- High blood pressure
- High cholesterol
- Poorly controlled type 2 diabetes

1.6 Motivation

Alzheimer’s disease (AD) is the most prevailing type of dementia. The prevalence of AD is estimated to be around 5% after 65 years old and is staggering 30% for more than 85 years old in developed countries. And it is very hard to find the symptom at the early stages. So, we got our motivation from here, to build a model which will detect the stages of AD from MRI Images and diagnosis.[1]

1.7 Thesis Overview

Alzheimer’s disease is an incurable, progressive neurological brain disorder. Earlier detection of Alzheimer’s disease can help with proper treatment and prevent brain tissue damage. Several statistical and machine learning models have been exploited by researchers for Alzheimer’s disease diagnosis. Analyzing magnetic resonance imaging (MRI) is a common practice for Alzheimer’s disease diagnosis in clinical research. Detection of Alzheimer’s disease is exacting due to the similarity in Alzheimer’s disease MRI data and standard healthy MRI data of older

people. We use deep learning techniques have successfully demonstrated human-level performance in numerous fields including medical image analysis. We also use a deep convolutional neural network for Alzheimer's disease diagnosis using brain MRI data analysis. While most of the existing approaches perform binary classification, our model can identify different stages of Alzheimer's disease and obtains superior performance for early-stage diagnosis. We conducted ample experiments to demonstrate that our proposed model outperformed comparative baselines on the Open Access Series of Imaging Studies dataset.[1

Chapter-02: BACKGROUND STUDY

2.1 Convolutional Neural Network

CNN is one of the key categories for image classification and image recognition in neural networks. It takes an image as input, which is classified and process under a certain category.

Each input image in CNN is processed by a series of convolutional layers, pooling, fully connected layers, and filters (Also known as kernels). The Soft-max function will then be used to categorize an object using probabilistic values between 0 and 1.

2.2 CNN Architecture

CNN primarily focus on the basis that the input will be comprised of images. This focuses the architecture to be set up in way to best suit the need for dealing with the specific type of data.

One of the most significant variations is that the layers of the CNN are made up of neurons that are organized into three dimensions, including depth and the spatial dimensionality of the input. The depth refers to the third dimension of an activation volume rather than the overall number of layers in the ANN.

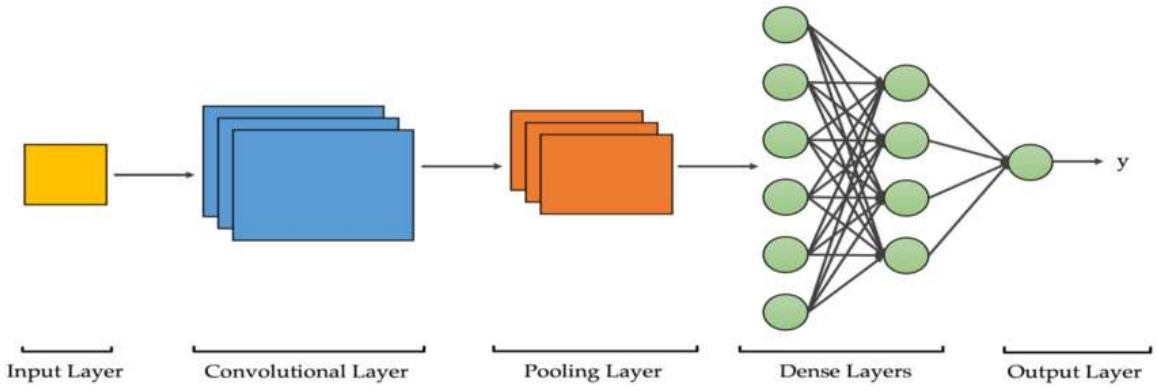


Figure 2.1: A basic CNN structure

There are three layers in a CNN architecture.

1. Convolution layer
2. Pooling
3. Fully-connected layer.

There are two main parts to a CNN architecture:-

1. A convolution tool that separates and identifies the various feature of the image for analysis in a process called Feature Extraction.

2. A fully connected layer that utilizes the output from the convolution process and predicts the class of the image based on the features extracted in previous stages. [3]

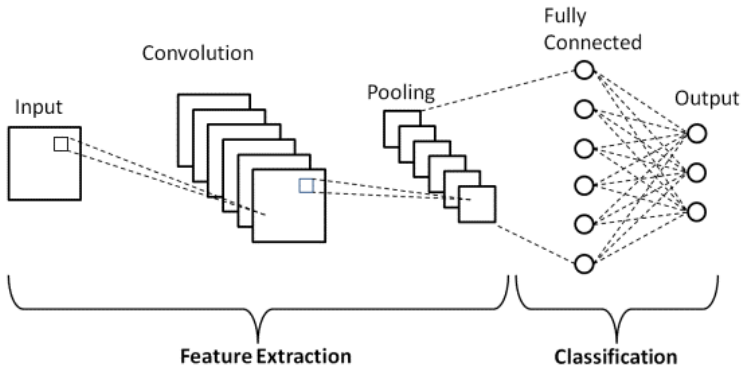


Figure 2.2: Configuration of CNN architecture

2.2.1 Convolution layer

Convolution layer is the first layer which extracts features from input which is an image. It preserves the relationship between pixels by learning image features using small squares of input data. It is a mathematical operation that takes two inputs such as image matrix and a filter or kernel. Convolution of an image with different filters can perform operations such as edge detection, blur and sharpen by applying filters. [4]

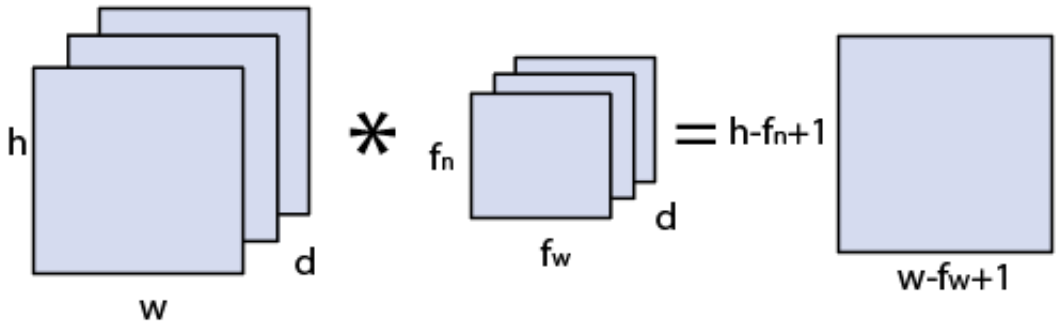


Figure 2.3: Image matrix multiplies kernel or filter matrix

2.2.2 Max pooling

A sample-based discretization technique is max pooling. Its major goal is to reduce the dimensionality of an input representation so that assumptions can be made about the features existing in the sub-region binned.

By using a max filter on non-overlapping sub regions of the initial representation, max pooling is accomplished. [4]

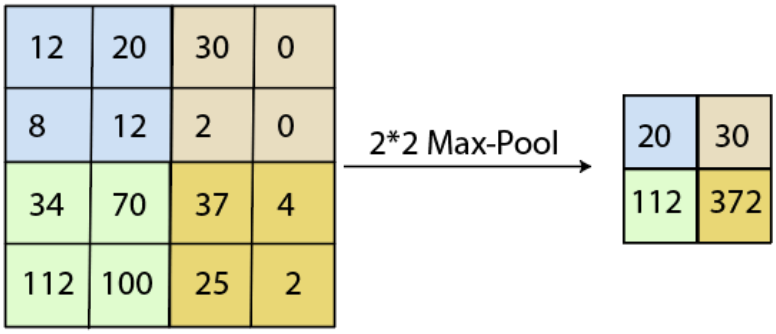


Figure 2.4: Max pooling

2.2.3 Fully-connected layer

Neurons in the fully connected layer have direct connections to the neurons in the two adjacent layers; they are not connected to any neurons in those layers. It makes up the network's final several levels. The last pooling or convolutional layer's output, which has been flattened, is sent into the fully connected layer as the layer's input. [4]

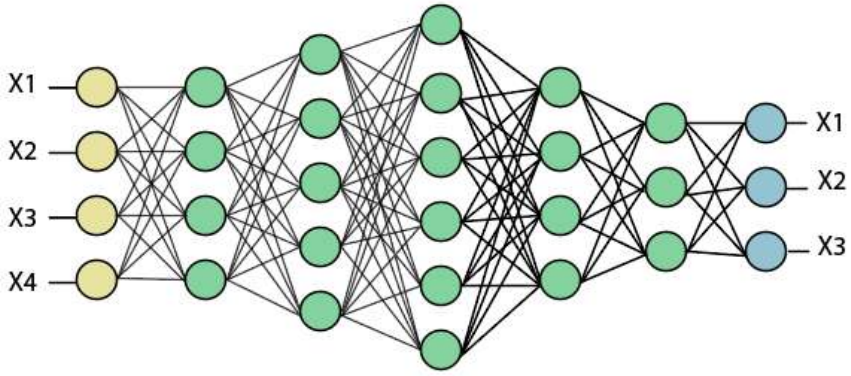


Figure 2.5: After pooling layer, flattened as Fully-connected layer

Chapter-03: LITERATURE REVIEW

Jyoti Islam and Yanqing Zhang [1] analyzed brain MRI data to diagnose AD. Their model provides significant improvement for multi-class classification and tested on AD dataset. They got 96% accuracy from their model.

Siqi Liu et al. [5] created a stacked auto-encoder deep learning architecture with a SoftMax output and used it on ADNI MRI data. They could accomplish it with prior knowledge of the domain and tagged training samples. In the classification of AD, they came up with an overall Accuracy score of 87.76%.

Christos Davatzikos et al. [6] have developed machine learning techniques to build classifiers using imaging data and clinical measures for AD diagnosis. They discovered major anatomical changes between the healthy brain and the brain affected by AD in areas like the entorhinal cortex and the hippocampal region.

Gopi Battineni et al. [7] used MRI data to build multiple machine learning models for predicting dementia in the elderly. People with mild atrophy, leukoaraiosis, and typical dementia cases of Alzheimer's disease were included in their study. Four machine learning models were trained by them. Combining all four models with chosen features improved dementia prediction accuracy. The accuracy was enhanced to 98% when all four models were combined with certain attributes.

AK Ambastha [8] said that there is a significant connection between the changes in brain tissues connectivity and behavior of AD patient.

Courtney Cocherane et al. [9] evaluated different pre-processing techniques, machine learning models, and feature selection strategies. They employed longitudinal lifestyle interventions as opposed to MRI data. In forecasting Alzheimer's disease, they were able to recollect information with more than 90% accuracy. They developed a "lean" diagnostic protocol that may accurately predict the onset of AD in a patient with three tests and four clinical visits, with a recall rate of 79% and an accuracy of 87%.

Manu Subramoniam et al. [10] proposed classifying Alzheimer's disease based on a deep neural network using Magnetic Resonance Images (MRI) as input for the classification task. They established that the VGG-16 performed better than the VGG-19 among the VGG architectures, Resnet-18, one of the residual neural network architectures, performed better than Resnet-101 in terms of accuracy.

Chapter - 04: Methodology

4.1 Dataset Used

For this study, we used the MRI image as a dataset from kaggle. Kaggle is an online community platform for data scientists and machine learning enthusiasts. Kaggle allows users to collaborate with other users, find and publish datasets, use GPU integrated notebooks, and compete with other data scientists to solve data science challenges.

We use total 6400 gray scale MRI Image which divided into two classes.

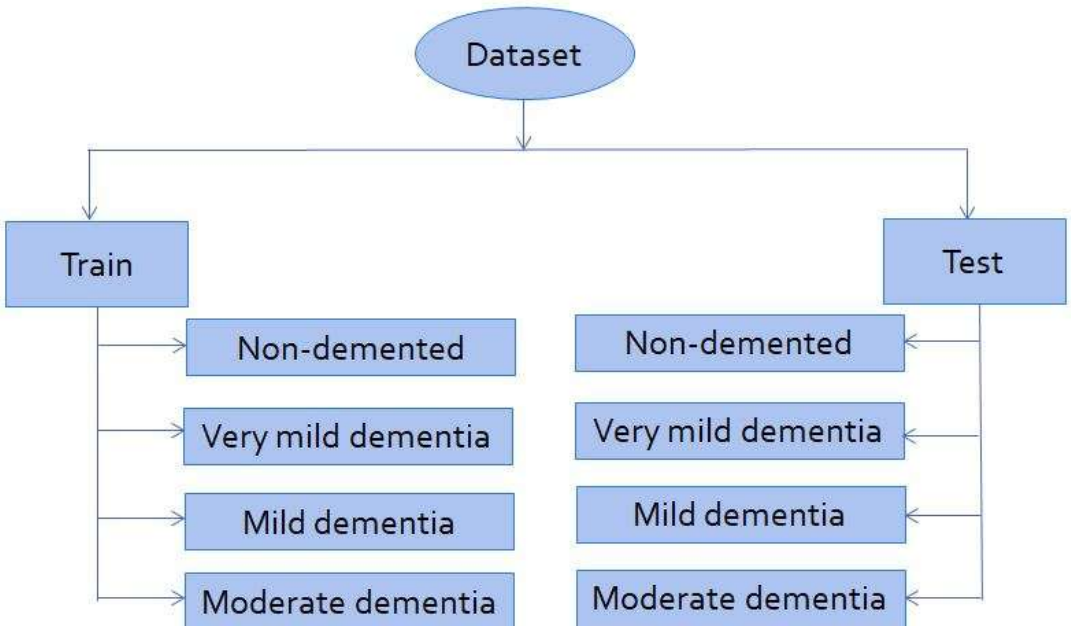
i. Train Data
ii. Test Data

Train data are divided into four classes:

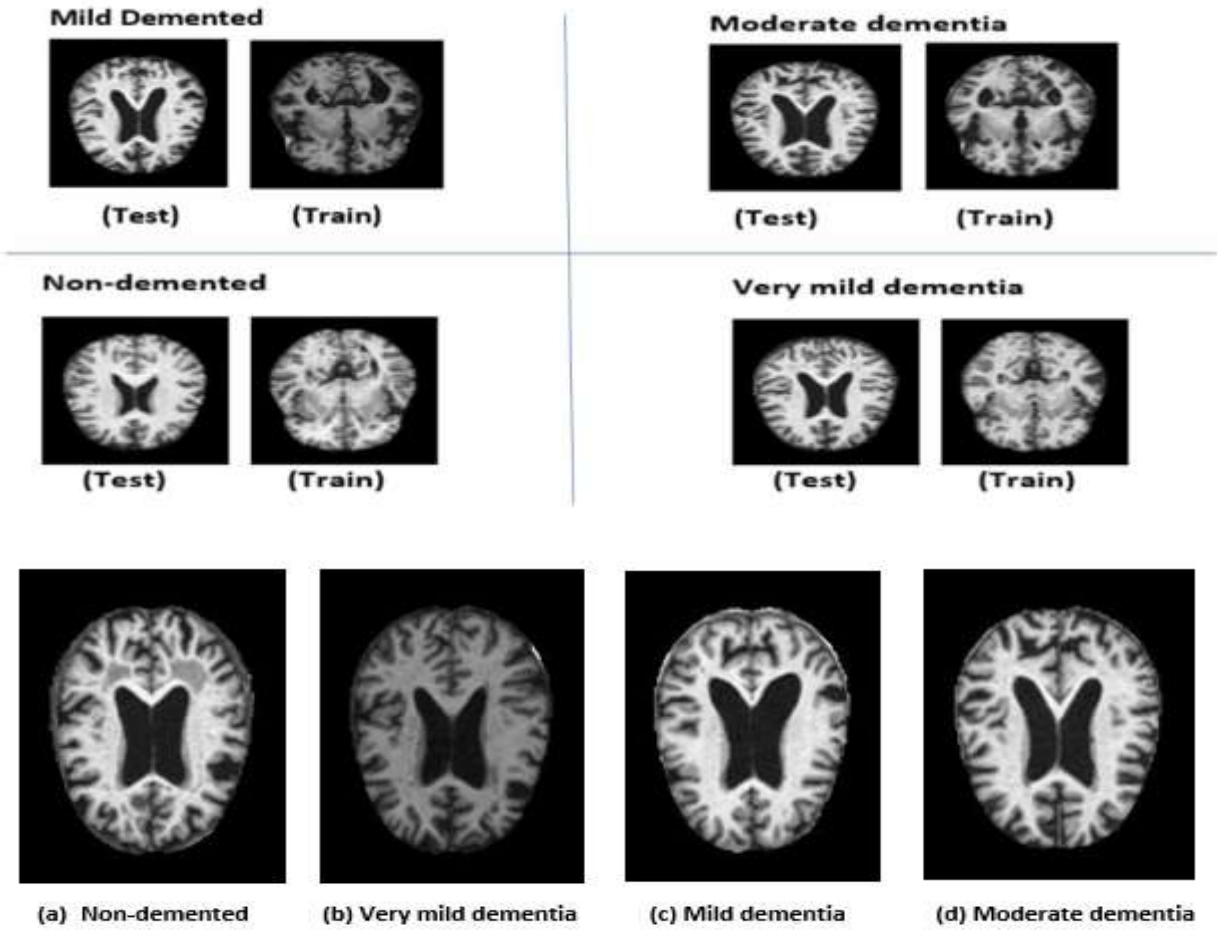
i. Non-demented
ii. Very mild dementia
iii. Mild dementia
iv. Moderate dementia

Test data are divided into four classes:

i. Non-demented
ii. Very mild dementia
iii. Mild dementia
iv. Moderate dementia



MRI Image:



4.2 Data Preprocessing

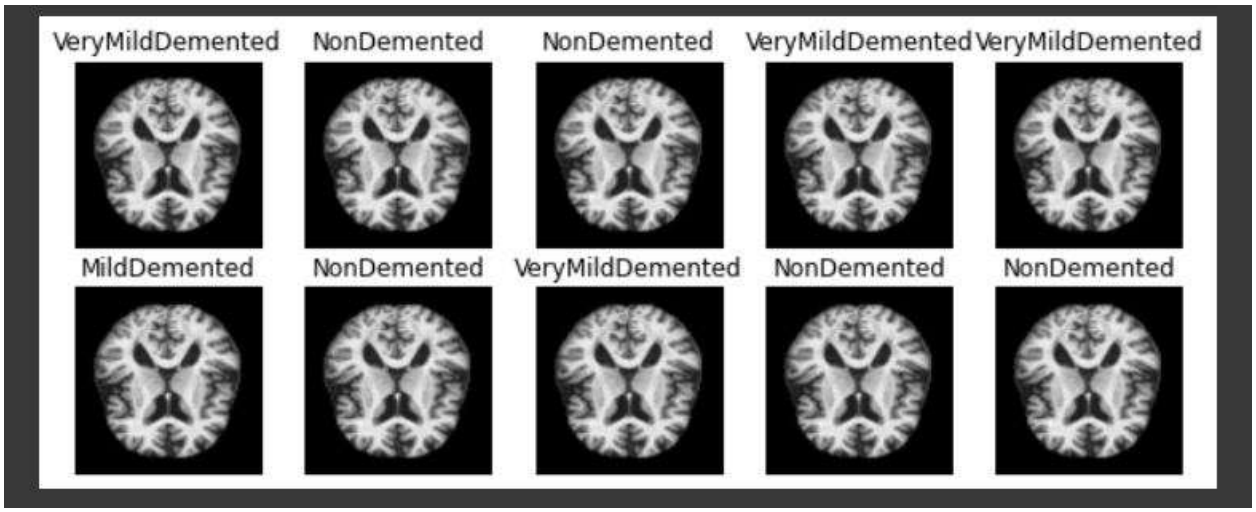
Data preprocessing can refer to manipulation or dropping of data before it is used in order to ensure or enhance performance, and is an important step in the data mining process. Our input image size 160 x 160. We apply CNN components for image classification. Firstly we divide into 3 parts of our data.

- Train Data
- Test Data
- Validation Data

For getting this output we use some arguments. Validation split = 0.2 which means that 80% of the data is used to train the model and the rest 20% will be used to test the model. So the loss and acc are calculated using 20% of the dataset.

Subset = 'training'. It is common to use a subset of the available historical data to train a model. This way we can compare multiple iterations during the model build process and pick the iteration with the lowest error.

Image size, batch sizes are also use. Then shuffle all the data and we get the output:



Here these 10 images shown us its take input image. And we get our total dataset output

```
Found 5121 files belonging to 4 classes.
Using 4097 files for training.
Found 5121 files belonging to 4 classes.
Using 1024 files for validation.
```

After that we print the total train data per batch and total validation data per batch and we get the output:

```
total train data per batch: 410
total validation data per batch: 103
(10, 160, 160, 1)
```

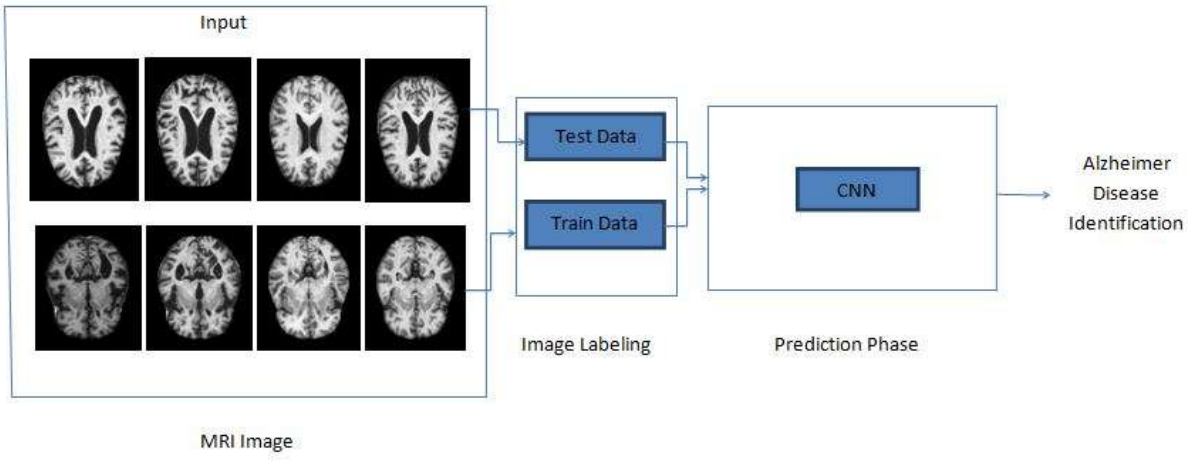
4.3 Deep Learning Algorithm

There is several Deep Learning Algorithms like:

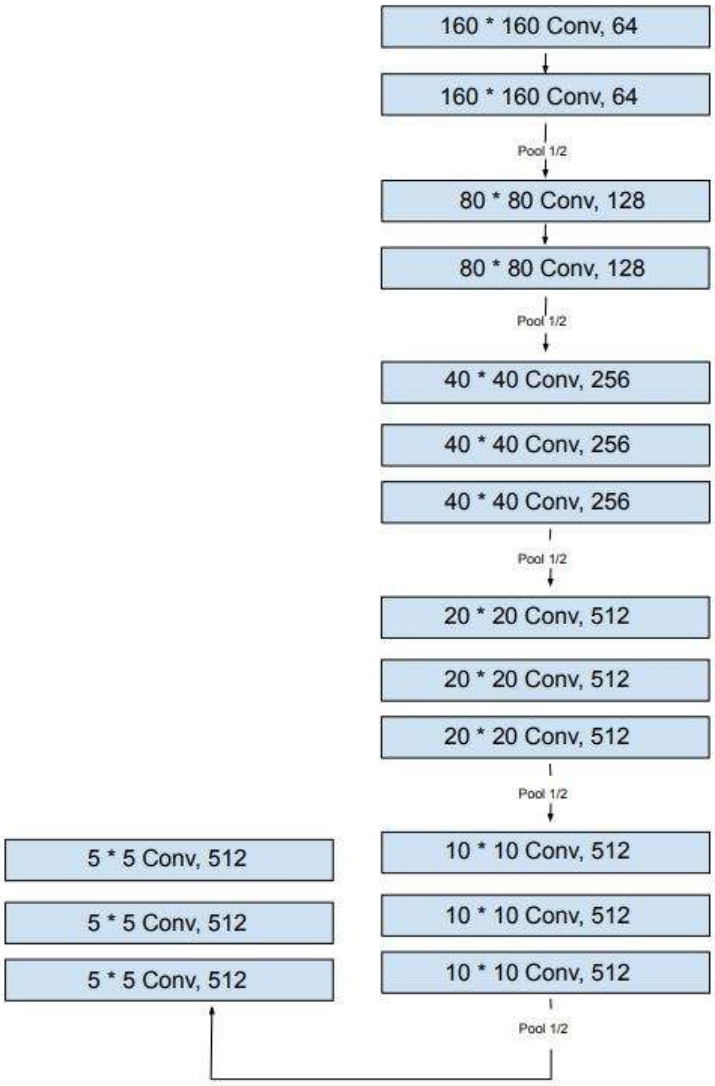
i. Convolutional Neural Networks (CNNs)
ii. Long Short Term Memory Networks (LSTMs)
iii. Recurrent Neural Networks (RNNs)
iv. Generative Adversarial Networks (GANs)
v. Radial Basis Function Networks (RBFNs)
vi. Multilayer Perceptrons (MLPs)
vii. Self Organizing Maps (SOMs)
viii. Deep Belief Networks (DBNs)

But for our work we use CNN.

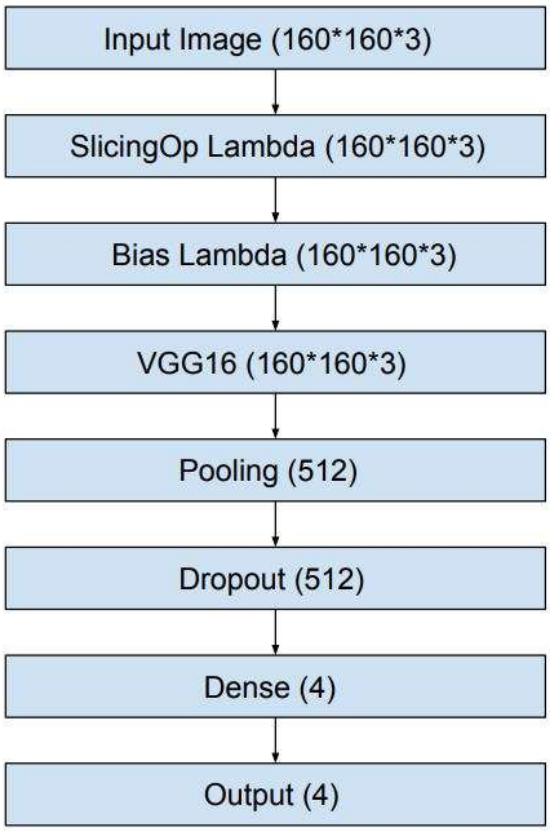
After processing our data, we moved onto selecting an efficient deep learning algorithm. Selecting the best machine learning algorithm is very important. So, we experimented with several deep learning algorithms. We used both classification and ensemble learner algorithms. Ensemble learners can sometimes perform better than the classification algorithms by combining the predictions of multiple base estimators. A CNN is a kind of network architecture for deep learning algorithms and is specifically used for image recognition and tasks that involve the processing of pixel data. There are other types of neural networks in deep learning, but for identifying and recognizing objects, CNN is the best choice because our complete work depends on MRI image. That's why we use CNN algorithm.



4.4 CNN Block Diagram



Here we can see that how CNN work on:



The dimension of the train image that we have taken in the input image is 160 x 160 x 3. Here 3 is image dimension. We use gray scale image so we need to take 160x160x1 but we take 3 because we use VGG16 model and in python there is pre build model called imagenet which will take input 3. 160 x 160 is image count. Here convolution layer start from input image size which means starting size is 160 x 160 x 64. After completing first convolution it will go down and its size decrease ½. Then the size will become 80 x 80 x 128. Here 64 is increase because after max pooling its take only those data that are needed but pooling increased that's why 64 become 128.

VGG 16 has 16 layers after convolution layer last 4 layers will be dense layer here output and dense layer will be same because dense layer always connected with output layer.

4.5 CNN Network Architecture

Our proposed network is an ensemble of three deep convolutional neural networks with slightly different configurations. We made a considerable amount of effort for the design of the proposed system and the choice of the architecture. All the individual models have a common architectural pattern consisted of four basic operations:

i. Convolution
ii. Max pooling
iii. Fully connected layer
iv. Output

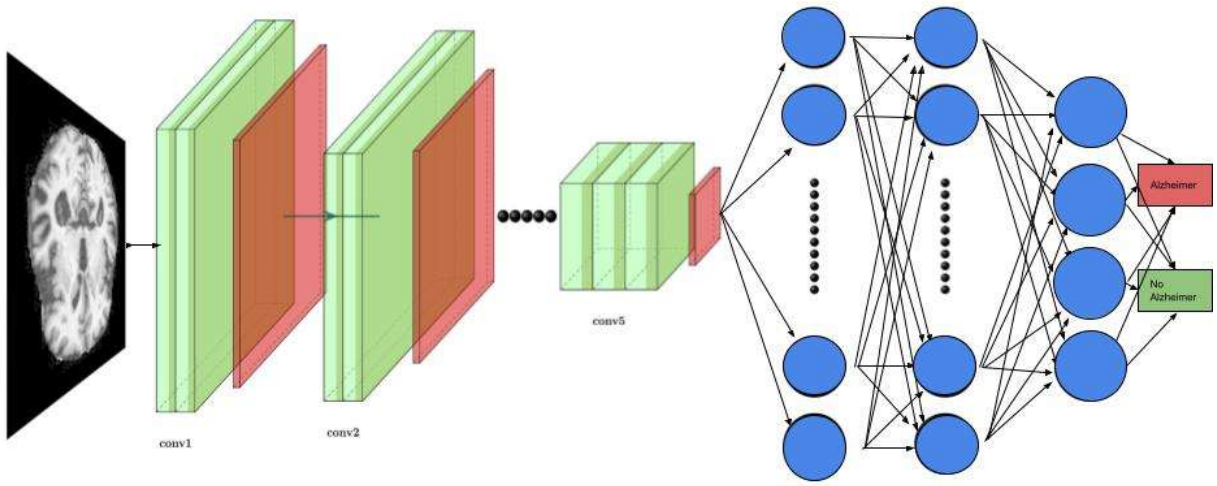


Figure 4.1: CNN Architecture

4.6 Experimental Settings

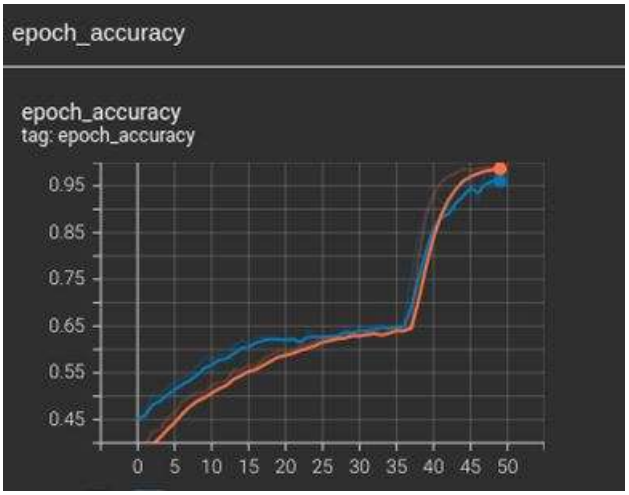
We implemented the proposed model using Tensorflow. Here, tensorflow is a free and open-source software library for machine learning and artificial intelligence. It can be used across a range of tasks but has a particular focus on training and inference of deep neural networks, Keras is an open-source software library that provides a Python interface for artificial neural networks. Keras acts as an interface for the TensorFlow library and Python on a windows 10 machine with 4 GB RAM and NVIDIA GeForce. We use python as programming language and Google collaboratory for coding.

To validate the effectiveness of the proposed AD detection and classification model, we developed two baseline deep CNN.

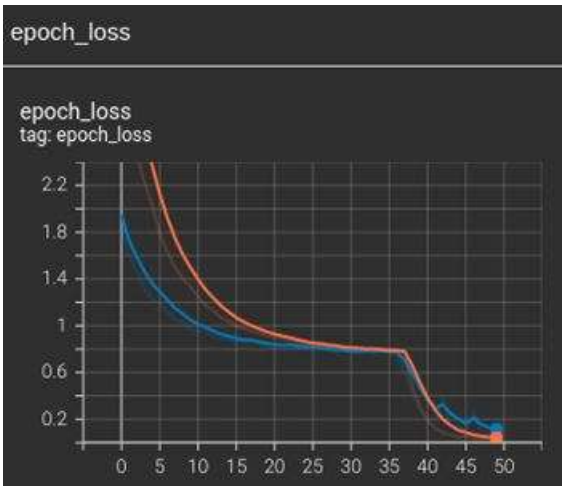
4.7 Accuracy graph

We get an accuracy flowchart which will show us how much accuracy we get.

Epoch accuracy:



4.8 Loss Data Graph:

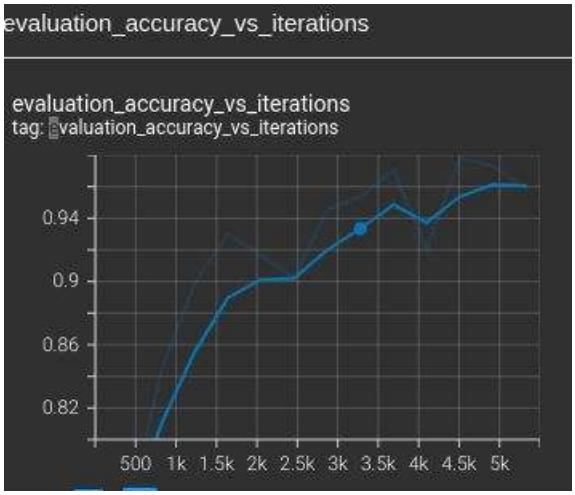


This graph will show us how many data we loss.

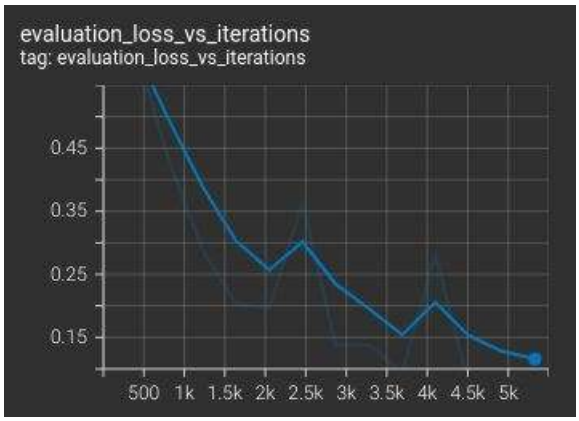
After getting epoch accuracy and epoch loss then we get the difference between evaluation accuracy vs iterations. Here evaluation accuracy is one metric for evaluating classification models. Informally, accuracy is the fraction of predictions our model got right.

Formally, accuracy has the following definition: Accuracy = Number of correct predictions Total number of predictions.

The graph is:



Then we get evaluation loss vs iterations which mean number indicating how bad the model's prediction was on a single example. If the model's prediction is perfect, the loss is zero. Otherwise, the loss is greater. The goal of training a model is to find a set of weights and biases that have low loss, on average.



4.9 AD Prediction Check:

Here we take one non demented image and get the same image as a prediction image. So we can say that our prediction is right.

Image 1:

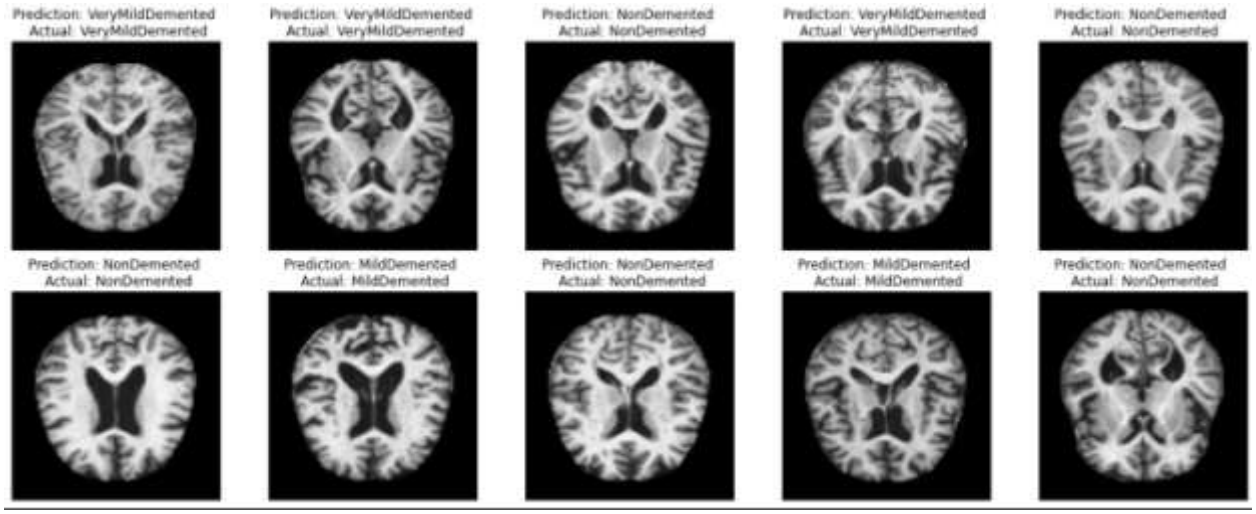
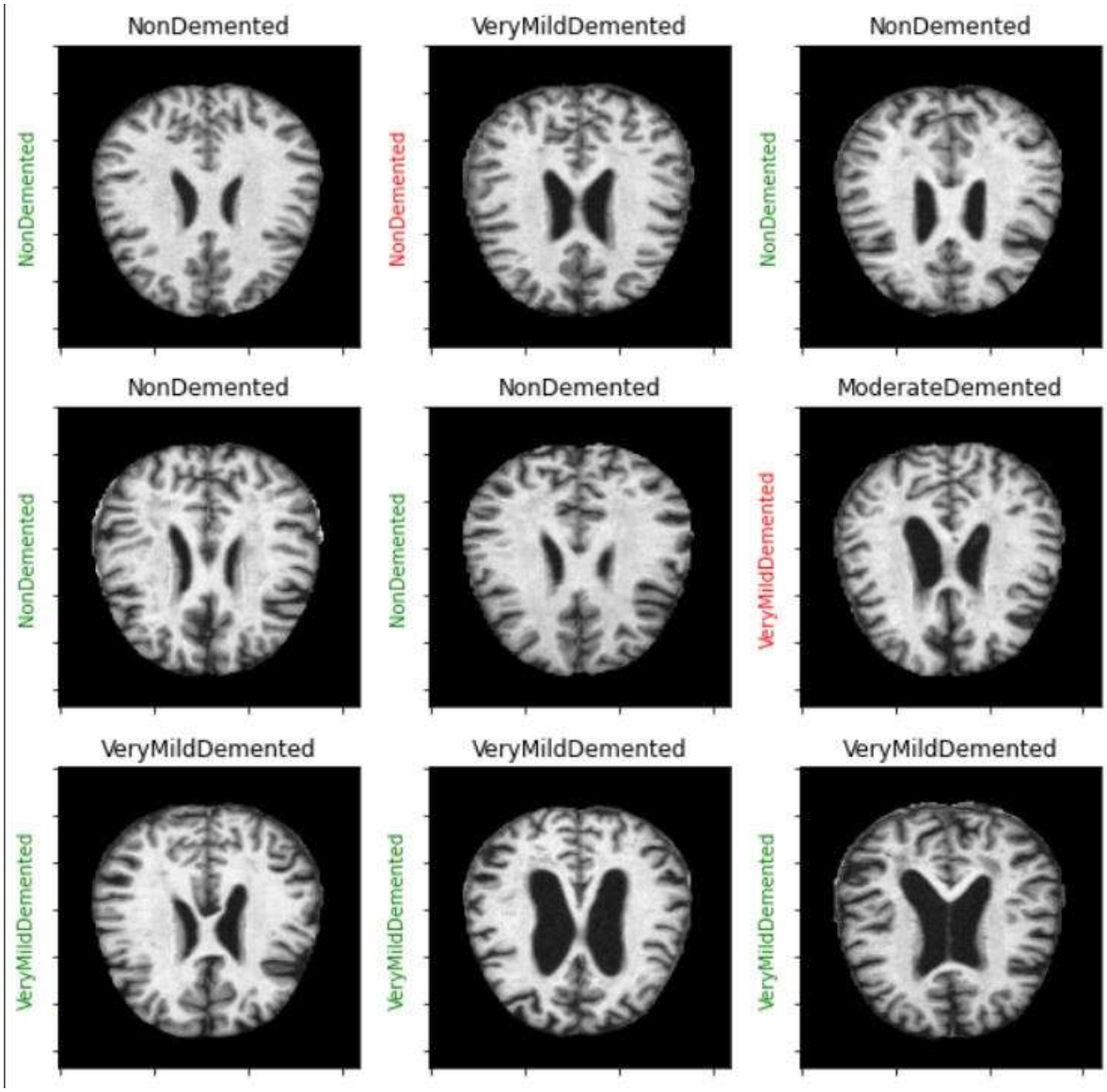


Image 2:


NonDemented
VeryMildDemented
NonDemented
NonDemented
NonDemented
NonDemented
NonDemented
NonDemented
ModerateDemented
NonDemented
VeryMildDemented
VeryMildDemented
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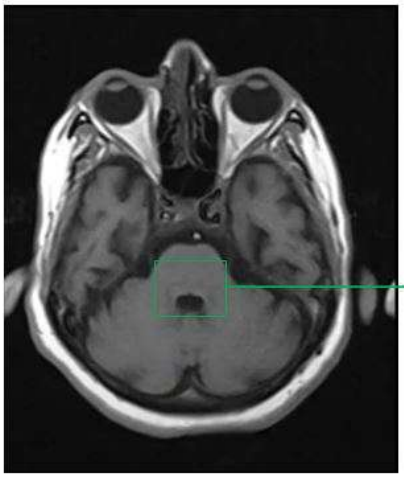
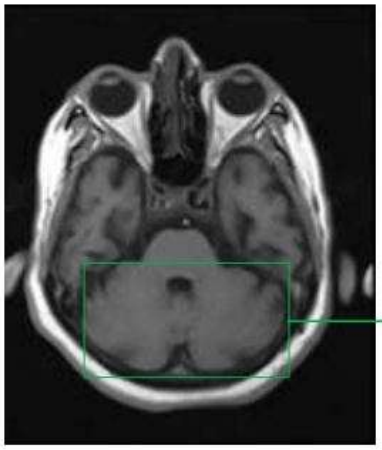
Patient Alzheimer's Analysis

Here we are discussing 70 years old female patient. This is a T1 sequence.

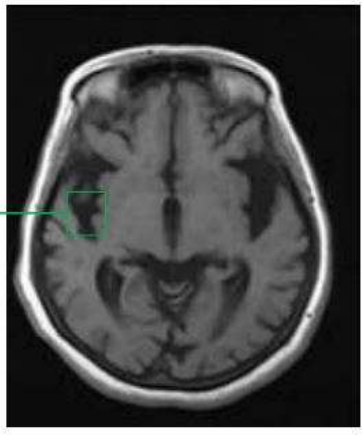


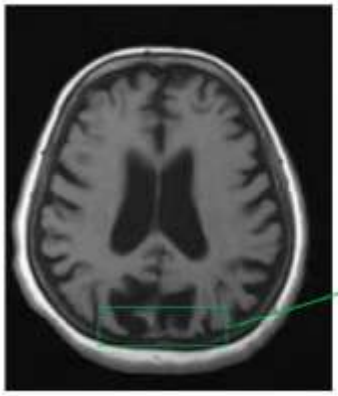
A normal brain stem

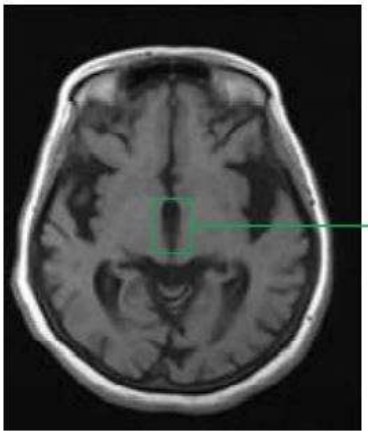


A normal cerebellar folial patterns

Prominent extra axial CSO spaces are noted around a long temporal lobe





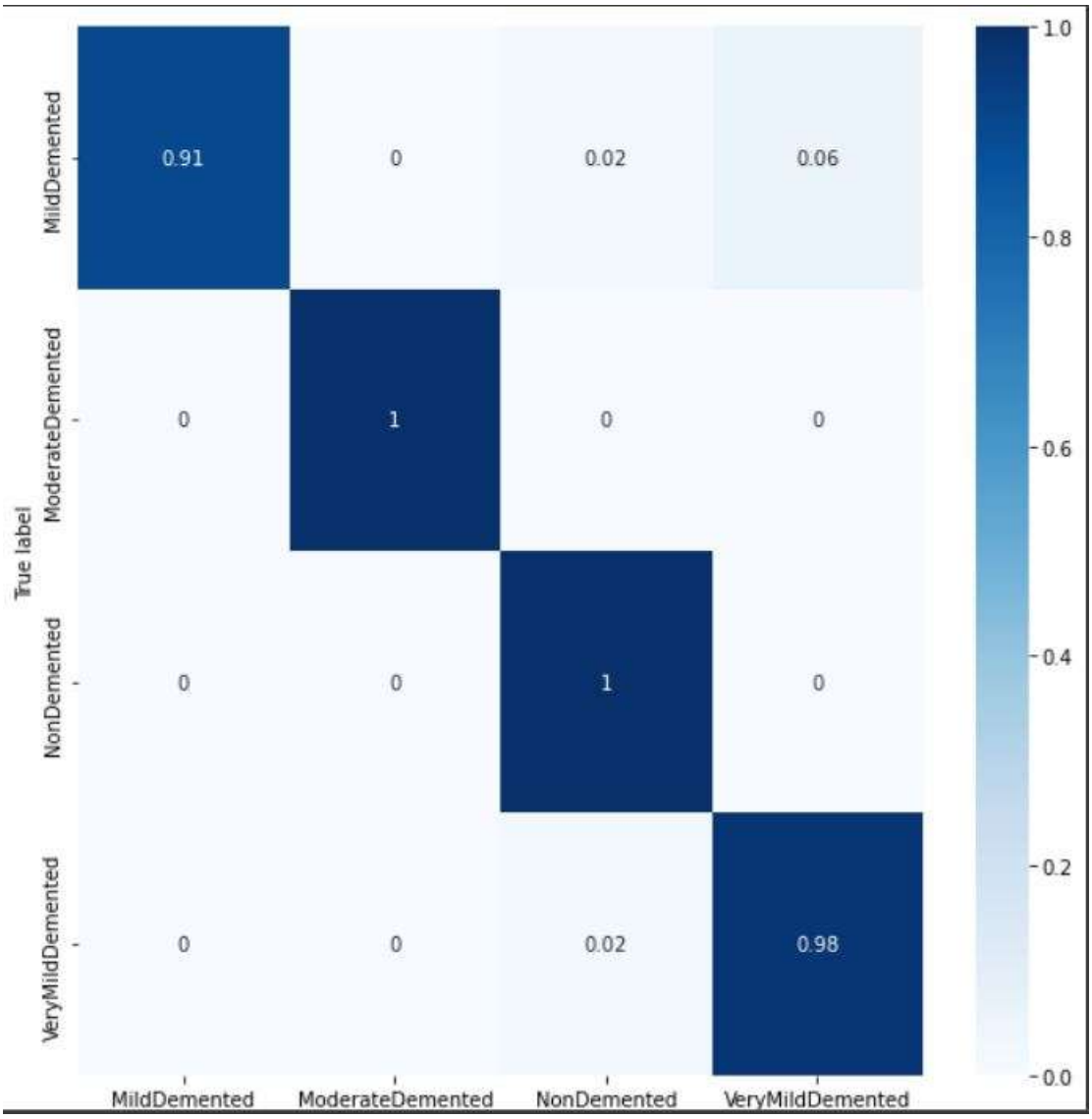


In this patient presented with the history of dementia and MRI has confirmed that changes in the brain represents Alzheimer's disease.

4.10 Confusion Matrix

A confusion matrix is a table that is used to define the performance of a classification algorithm. A confusion matrix visualizes and summarizes the performance of a classification algorithm. It is a useful machine learning method that allows you to measure recall, precision, accuracy, and AUC-ROC curve. Metrics are used for quantitative evaluation and comparison, including accuracy, positive predictive value (PPV) or precision, sensitivity or recall, and the harmonic mean of precision and sensitivity

Our confusion matrix diagram is given bellow:



4.11 Classification Performance Table

Class	Accuracy:
Mild demented	91%
Moderated	100%
Non demented	100%
Mild demented	98%

Chapter 5: Experimental Result & Discussion

5.1 Result

We report the classification performance model and see that we get mild demented 91%, moderated 100% non demented got 100% and very mild demented got 98% accuracy. This table shows the per-class classification performance of our proposed ensemble model on the kaggle dataset. The performance comparison of classification results of the proposed ensembles model with deep CNN network. We use a large data set that's why we get the best accuracy because without a large dataset, training process would not work correctly. On the other hand, the depth of our model is relatively high, and all the layers are connected to all preceding layers. We propose a deep convolutional neural network that can identify Alzheimer's disease and classify the current disease stage. After completing full process we get the total accuracy which is 97.84%. **So our final accuracy is** 97.84%.

Then we find the Training data accuracy and loss, Training and Validation Accuracy and Training and Validation Loss. We apply CNN to find the accuracy. The accuracy of the proposed model is 97.84%. which is better than previous existing accuracy model which is 93.18% with 94% precision, 93% recall and 92% f1-score.[11] After that we plot some graph which will shown us how to Training data accuracy and loss, Training and Validation Accuracy, Training and Validation Loss. Then we plot a table called confusion matrix in deep learning algorithm which will give us this output.

5.2 Conclusion

We made an efficient approach to AD diagnosis using brain MRI data analysis. While the majority of the existing research works focuses on binary classification, our model provides significant improvement for multi-class classification. Our proposed network can be very beneficial for early-stage AD diagnosis. Tough the proposed model has been tested only on AD dataset we believe it can be used successfully for other classification problems of medical domain. Moreover, the proposed approach has strong potential to be used for applying CNN into other areas with a limited dataset. Overall, on the basis of high-level literature review, we found that the published papers in this area tend to focus on two main areas of research, namely, biomarkers and neuro imaging, but with increasing interest in image analysis. Although regarded thorough and extensively conducted, the work adds little knowledge to the initial detection of AD, as the majority of selected patients are already known to have AD. This study reviewed the some of the important related AD datasets and diagnoses techniques and detection. This approach is feasible for early-stage neuro imaging research.

5.3 Future Work

In future, we plan to evaluate the proposed model for different AD datasets and other brain disease diagnosis.

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