Detection of Alzheimer's Disease

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Abstract- *Alzheimer's disease (AD) is a commonly known and widespread neurodegenerative disease which causes cognitive impairment. Although in medicine and healthcare areas, it is one of the frequently studied diseases of the nervous system despite that it has no cure or any way to slow or stop its progression. However, there are different options (drug or non-drug options) that may help to treat symptoms of the AD at its different stages to improve the patient's quality of life. As the AD progresses with time, the patients at its different stages need to be treated differently. For that purpose, the early detection and classification of the stages of the AD can be very helpful for the treatment of symptoms of the disease. On the other hand, the use of computing resources in healthcare departments is continuously increasing and it is becoming the normal to record the patient' data electronically that was traditionally recorded on paper-based forms. This yield increased access to a large number of electronic health records (EHRs). Machine learning, and data mining techniques can be applied to these EHRs to enhance the quality and productivity of medicine and healthcare centers. But still, they have never given compromising results. Thus, Deep Learning (DL) has become a common technique for the early diagnosis of AD. Here, we tried various deep learning techniques and compared thier accuracies and found a most suitable model for early detection of alzheimer's disease.*

I. INTRODUCTION

Translational applications of computational neuroscientific approaches have been proven exceptionally beneficial in comprehensive mental health trials. This multidisciplinary field of study can help model the biological processes governing the healthy and diseased states of the human brain and map these processes into observable clinical presentations. In the past decade, the rapid increase in high-volume biomedical datasets (neuroimaging and related biological data), concurrent with the advances in machine learning (ML), has opened new avenues for the diagnosis and prognosis of neurodegenerative and neuropsychiatric disorders. From a computational perspective, this recent advancement has spawned the development of tools that incorporate several patient-specific observations into predictions and improve the clinical outcomes of patients suffering from such disorders,. The ultimate purpose of these neuroscientific approaches is to enhance the initial exposure and complete the treatment plan of individuals in high risk of Alzheimer's disease (AD) and AD-related cognitive decline.
For the reasons mentioned above, recent studies have focused on establishing exceptionally capable approaches that use ML systems to enhance the examination of AD. The use of automatic systems capable of differentiating pathological cases from normal cases based on their magnetic resonance imaging (MRI) scans (i.e., no past hypotheses are needed) will contribute immensely to the initial diagnosis of AD.

1.1 ALZHEIMER'S DISEASE STORY

The history of AD, as presented in this section, is consolidation of finding from AD publications searched in Google Scholar. Only the latest publications were considered, and only the papers published between 2008 and 2019 were selected. Our research focused on datasets used to examine AD and mild cognitive impairment MCI), the forerunner of AD. The processes and techniques used by previous researchers were studied.

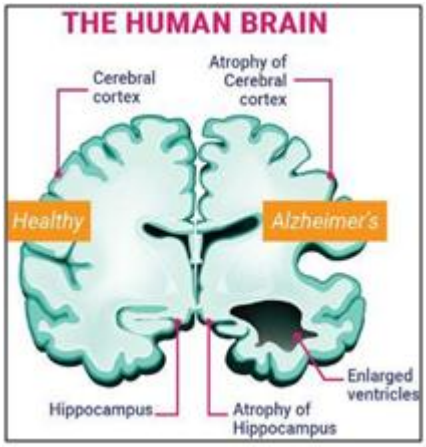
1.2 ALZHEIMER'S DISEASE

In 1997, Dr. Gerber and his colleagues from the Psychiatric Department of Max Planck Institute of Neurobiology examined histological cuts from F. Johan whose brain tissues had been well preserved for over 90 years. The research was regarded the second reported case of AD. An examination of the cuts revealed numerous amyloid plaques. The above research suggests that a mutational analysis of preserved brain tissue is practicable. On the 100th anniversary of Dr. Alzheimer's historic discovery, his findings were again confirmed. Figure

1.1 shows a comparison of a healthy brain and a brain affected by AD

AD is currently ranked as the sixth leading cause of death in the US. Recent estimates indicate also that the disorder may even rank third (after heart disease and cancer) as the leading cause of the death for elderly. Clearly, predicting the progression of AD at its early stages and preventing the disease from progressing are of great

importance. The diagnosis of AD requires various medical tests and enormous multivariate heterogeneous data.



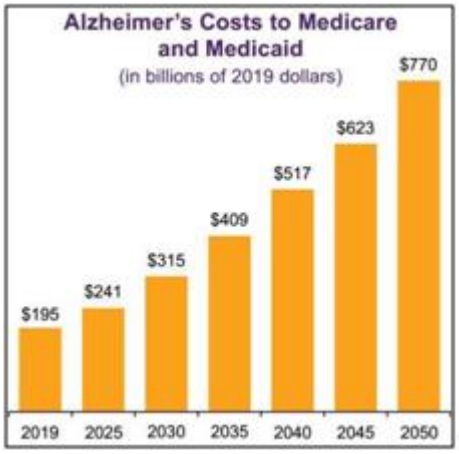


Fig 1.1 Progress of AD from MCI to severe AD

manual comparison, visualization, and analysis of data are difficult and tedious due to the heterogeneous nature of medical tests. An efficient approach to accurately predict brain conditions is by classifying MRI scans, but this task is also challenging. Nonetheless, novel approaches have been proposed to diagnosis AD at its early stages through the efficient classification of brain MRI images and the use of label propagation with convolutional neural network (CNNs). As reported by the Alzheimer's Association in 2019, treatment for AD remain unavailable. In US alone, over five million people are affected by AD; amongst them, 200,000 individuals are younger than 65 years old. The report indicates that AD is expected to affect 10 million people, most of them in their 60s by 2050. This report further says that someone is affected with AD every 67 seconds. Figure 1.2 shows the estimation of Alzheimer's costs (in USD millions) of Medicare and Medicaid within the coming 50'syear.

1.3 BRAIN IMAGING TECHNIQUES FOR ALZHEIMER'S DISEASE

Brain imaging techniques can be used to non-invasively visualize the structure, function, or pharmacology of the brains. The imaging techniques are generally divided into two categories: structural imaging and functional imaging. Structural imaging provides information about the brain's structure, including neurons, synapses, glial cells, etc.

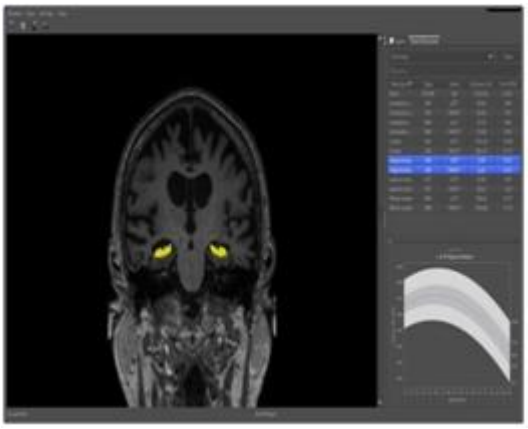


Fig 1.3 Example Of Structural Magnetic Resonance Imaging (MRI)

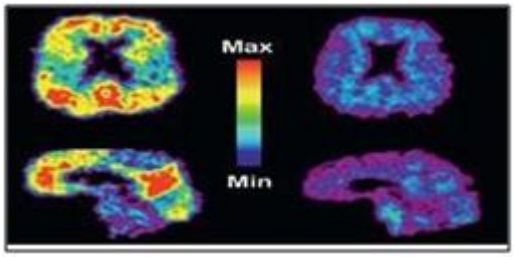


Fig 1.4(a) The Brain Area In Older

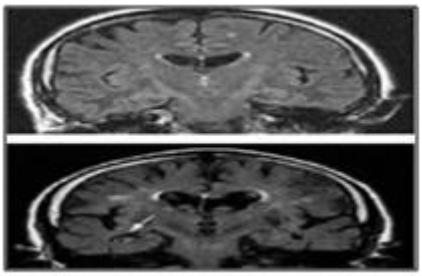


Fig 1.4(b) MRI Scan Brain In Medial Temproral Atrophy

Functional imaging provides information about the activities performed by the brain. The neuroimaging techniques mostly used for AD are the following:

1.3.1 MAGNETIC RESONANCE IMAGE(MRI)

This imaging technique utilises radio waves and magnetic fields to generate high-quality and high-resolution 2D and 3D images of brain structures. No harmful radiations from X-rays or radioactive tracers is generated. The most commonly used MRI for AD cases is the structural MRI,

which measures brain volumes in vivo to detect brain degeneration (loss of tissue, cells, neurons, etc. Brain degeneration is an inevitable progressive component of A. Fig 1.3 shows an example of a structural MRI used to detect brain atrophy. Alternatively, Fig. 1.4 shows an example of functional Magnetic Resonance Imaging (fMRI), a widely used method to measure human primary visual cortex and detect brain topography. fMRI provides useful information and data about the human brain's activity, i.e., how the brain functions.fMRI methods, such as brain imaging based on arterial Blood Oxygenation Level Dependent BOLD) contrasts and spin- labelling (ASL), are sensitive to the cerebral metabolic rate of oxygen consumption and cerebral blood flow (CBF). Fig 1.4(a) shows the brain areas of elderly subjects (AD patients; control), whilst Fig 1.4(b) shows medial temporal activation for the same control group.

Compared to other techniques, Single-Photon Emission Computed Tomography (SPECT) is more economical than the other techniques, but it is particularly delicate for the initial examination of changes in cerebral blood flow. However, this technique remains to be one of the most popularly used procedures when analysing cerebral functions. Many studies have shown that SPECT can precisely measure the cerebral perfusion of patients during AD examination.

1.3.2 POSITRON EMISSION TOMOGRAPHY(PET)

This imaging procedure utilises radiotracers, and the brain's activities are analysed as radioactive spheres. Figure 1.5 shows the use of amyloid and flfluorodeoxyglucose, the most commonly used tracers, for AD diagnosis.

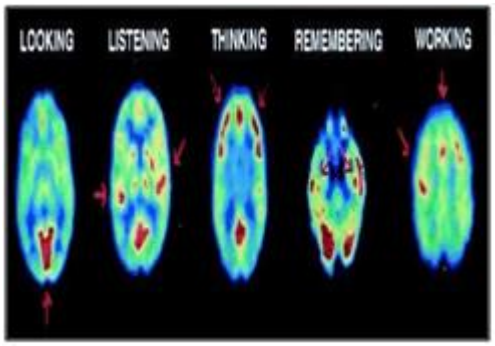


Fig 1.5 PET Sscan Of A Brain In Normal Condition

1.3.3 MRI BIOMARKERS OF AD

Biomarkers are regarded as the medical signs (i.e. the external manifestations of the medical statuses of patients) that can be measured precisely. Biomarkers are defined in many different ways. For example, the International Program on Chemical Safety defines a biomarker as an object, an architecture or a procedure for a body that can be measured and from which the presence of a disorder can be concluded. AD biomarkers have the following properties:

- Capable of identifying basic characteristics of AD's neuropathology;
- Capable of certifying neuropathologically confirmed AD cases;
- Efficient, capable of identifying initial AD and capable of differentiating AD from different forms of dementias;

Reliable, non-invasive, easy to implement and inexpensive. Three kinds of biomarkers can help further describe AD: genetic, biochemical and neuroimaging biomarkers.

1.4.1 OBJECTIVES

1.3.4 The main objective of this project is to build a simple yet complete representative of prediction of Alzhiemer's disease detection.

A distinct classifier is used by this project to predict whether or not a patient will have Alzhiemer disease at thier earlier stage. The dataset has MRI images and it's multiclass prediction. The aim is to predict the likelihood of alzhiemer disease at the early stages using MRI image dataset.

1.3.5 The goal of this project is to create a technology that can to propose a generalized and useful Deep learning technique for early diagnosis of Alzheimer's disease using magnetic resonance imaging (MRI) images with expected high accuracy.

1.3.6 ... This research also aims to suggest an important approach for early Alzheimer's disease diagnosis.

1.4 MOTIVATION

The drastic spike in Alzhiemer's disease pushes for innovative analysis. The present incarnation of alzhiemer's individuals suffering from this disorder is the primary source of inspiration. The primary cause of the type of alzhiemer occurs in old aged individulas usually crosses the age of 65years. We want to build a device that could serve as a source of alzhiemer diagnosis for medical professionals on time and at thier early stages. So now the patient can better control his/her disease. Eventhough once an individual attains the alzhiemer disear it's not curable but the process can be completely slow down from becoming worse.

1.5 PROBLEM STATEMENT

Machine learning gained a significant position in healthcare services (HCS).However, early prediction of diabetes is quite challenging task for medical practitioners due to complex interdependence on various Factors as diabetes affects human organs such as kidney, eye, heart, nerves, foot etc. In Diabetic Retinopathy the Identification and Classification of input images proposes a big challenge to make machine more accurate. classify the i/p with higher rate of accuracy is challengeable. dominates) In this study, we have proposed an automatic prediction of Alzhiemer Disease using a deep convolution neural network based pre-trained transfer models and MRI brain images. For this purpose, we have used ResNet50, ResNet101, ResNet50V2, ResNet101V2, InceptionV3 and Inception- ResNetV2 pre-trained models to obtain higher prediction accuracies for three different mutliclass datasets including MRI images Non-dementia, Very Mild Dementia, Mild Dementia and Moderate Dementia of patients.

II. LITERATURE SURVEY

2.1 RELATED WORKS

Various literature papers were studied and analyzed to understand their work and techniques. ML has been used in the past decade to detect the MRI biomarkers of AD. Many ML methods are currently utilised to improve the determination and prediction of AD. A precise categorisation of stable MCI versus progressive MCI was achieved by Haller et al. by analysing 35 cases of normal controls and 67 cases of MCI with a support vector machine (SVM) [1]. Segmentation has been emphasised in most ML processes for bio-image classification, whereas the retrieval of strong texture descriptions has generally been neglected. Nonetheless, in many cases, retrieving compelling characteristics from a complete image can obviate the need for image segmentation [2]. Most of the early research used classic texture descriptors, such as Gabor filters and Haralick texture features [3], [4]. DL has been described as 'a new area of ML research, which has been introduced with the objective of moving ML closer to one of its original goals: artificial intelligence'

The DL structure typically involves more than two levels of abstraction and representation to help understand text, sound and image data [5]. DL can be classified into two sections, namely, generative architecture and discriminative architecture, as shown in Figure 9. Generative architecture can be subdivided into the four sections of Recurrent Neural Network (RNN), Deep Auto-Encoder (DAE), Deep Boltzmann Machine (DBM) and Deep Belief Networks (DBN), whilst discriminative architecture can be divided into Convolutional Neural Network (CNN) and RNN.
Researchers in the recent past have identified the scale-invariant feature transform and the local binary patterns as the modern texture descriptors for bio-image analysis [6]–[8]. As these descriptors are developed by humans to retrieve features from images, they are termed handcrafted features. As a type of classifier the SVM then receives the descriptions retrieved by the handcrafted procedure [9]. The most suitable descriptors retrieve descriptions from a dataset, and many of the most commonly used and compact descriptors use DL to accomplish the desired goal [10], [11]. For this purpose, the CNN is used to retrieve the descriptions from the images. CNNs act especially as a generic characteristics retriever [12].

Once a deep network is trained on a large volume of images, multiple levels of representations are produced. The first-layer features, for instance, resemble Gabor filters or colour blobs that are often generalizable on many other image problems and datasets [13].

Deep neural networks may be used with bio-image datasets, but this approach requires enormous amounts of data, which in most cases is hard to obtain [14]. The data augmentation process is the solution to this issue, as it has the ability to develop the data by customising the initial data through the application of its own procedure. Some of the well-known procedures of data augmentation are reflflecting, translating and rotating initial images to produce contrasting depictions [15]. Furthermore, different images can be obtained by customising the image's brightness, saturation and contrast [16], [17]. In addition to data augmentation, the other most commonly used method is the principal component analysis (PCA) jittering. In PCA jittering, some fundamental segments are added as they are multiplied by a lesser number [18], [19]. The main reason behind this process is to show only the most compatible characteristics of an image. In the latest research [20], [21], generative adversarial networks are utilised to blend images that contrast with the basic ones. This method requires the training of a distinct network [22], [23].

However, the produced images are not based on the changes in the image dataset. Other methods are therefore selected on the basis of the problem. For example, in [24], pointwise multiplications are utilised for the synthetic-aperture radar images to duplicate speckle noise. In [25], elastic deformation is adopted to reproduce the act of stretching in breast cancer treatments

Another way of exploiting DL is to fine-tune a pre-trained DL model, such as CNNs, on a new dataset representing a new problem. This approach exploits the

shallowest layers of a pre- trained CNN. Fine-tuning (or tuning) is a procedure that continues the training process on a new image dataset. This method greatly reduces the computational costs involved in the training process of new datasets, and it is suitable for relatively small datasets. Given the reduced computational costs, another benefit of using fine-tuning is providing opportunities to researchers to investigate easily the ensembles of CNNs. These ensembles can be built using more than one pre-trained CNN and many different parametric sets.

Other studies have employed CNNs merely as feature extractors [25]. The classification is undertaken using either SVM with a polynomial or linear kernels and logistic regression extreme ML random forest or XGBoost and logistic regression (decision trees) or SVM with various kernel [26]. The results retrieved from CNN classification and those from other classifiers that merely considered features extracted by CNN were compared by Shmulev and Belyaev [27]; they concluded that the latter operates more efficiently than the former. CNNs can be used on pre-extracted features instead of applied directly to image data. This case is especially true the CNN is directly applied to the outputs of various regression models or when clinical scores are compared with other hyper parameters and MRI-based features.

Additionally, CNNs can be applied to non-Euclidean spaces, such as patients' graphs or cortical surface images. Other architectures can also be applied to anatomical MRIs. Various studies have employed different versions of the multilayer perceptron, which consists of a probabilistic neural network or a stack of FC layers. Both supervised (deep polynomial networks) and unsupervised (deep Boltzmann machine and AE) structures have been employed by other studies to extract high-level representations of the features, whereas SVMs are primarily used for classification [28].

Extensive preprocessing, which usually occurs in non-CNN architectures, are applied to imaging features, such as texture, shapes or cortical thickness and regional features. Besides, embedding or feature selection is frequently required to further reduce dimensionalities. However, DL-based classification approaches are not restricted to cross-sectional anatomical MRIs only. Longitudinal studies can utilise information obtained from different time points whilst studying the same subject.

Nho et al. [29] implemented an SVM with kernels that allowed for the switching of amnestic MCI to AD whilst removing the other subtypes of the prodromal phase of AD. A 90.5% cross-validation efficiency was achieved in their AD and NC analyses. In addition, they achieved 72.3% efficiency in anticipating the progression of MCI to AD. Two processes were used for the retrieval of characteristics:

- FreeSurfer: a brain segmentation and cortical parcellation software tool.
- SPM5: a statistical parametric mapping tool.

In 2018, Liu et al. [30] suggested the use of cascaded CNNs because of their ability to progressively analyse different levels and characteristics of MRI and PET brain images. No expertise was required, as no image segmentation was involved in preprocessing the data. This feature generally serves as the advantage of this approach over the other methods. In the other methods, the features are retrieved and then fitted to the model. Their study involved 100 NC cases, 93 AD patients and 204 MCI patients based on the ADNI data. A 93.26% efficiency was achieved.

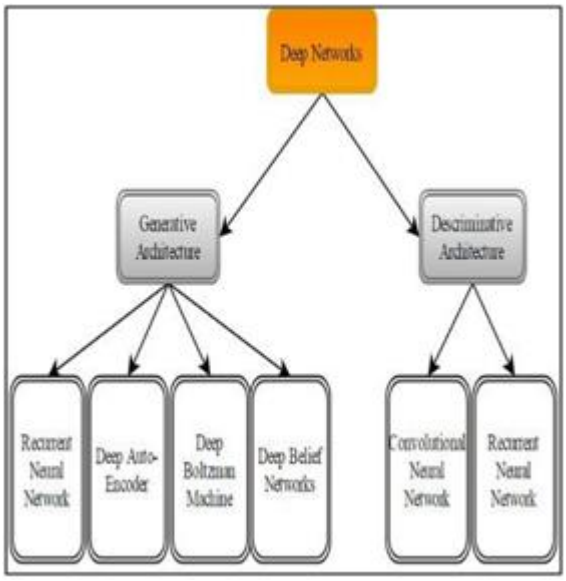


Fig 2.1 Categories Of Deep Learning Architectures

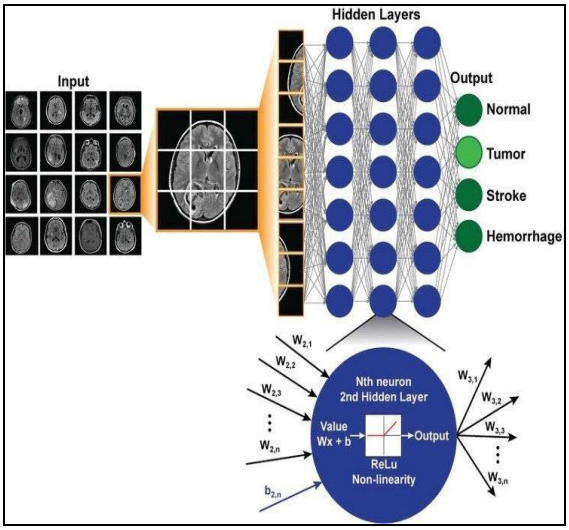


Fig 2.2 An Example Of Convolutional Neural Network (CNN) [48]

REVIEWS ON FINDINGS

- The Methodology used (Pre –Processing and Classifiers)
- The Classification algorithms performance metrics
- Merits and Limitations of the study about Alzhiemer Disease prediciton
- The Classification algorithms performance metrics
- we adapt several CNNs Transfer Learning (Inception V3, ResNett50, ResNet101, ResNet50V2, ResNet101V2, Inception-ResNet V2) for Alzhiemer"s Disease stage classification
- Alzhiemer disease diagnosis and detection has been accomplished by various pre- processing, classification as classifiers, model performance and evaluation, prediction using machine learning techniques and exceptional precision in detection.

DATA SOURCES USED

The Datasets are used from public and open-source platforms like kaggle, etc.

S.No	Tends to require Database (Dataset)
1	Alzheimer's Disease Detection from kaggle
2.	Alzheimer's Disease Neuroimaging Initiative
3.	The Open Access Series of Imaging Studies

Table 2.1 Data Sources used

2.2 SUMMARY OF LITERATURE SURVEY

Survey on Prediction of alzheimer disease based on deep learning using Artificial Intelligence is still evolving, due to the difficulty of appropriate precision synopsis and modelling. Different scholars and researchers are working hard to find a full suitable method of classification, using multiple techniques. The results from this study will support the same with individual deep learning pretrained models accuracy. Alzheimer disease diagnosis and detection has been accomplished by various pre-processing, classification as classifiers, model performance and evaluation, prediction using deeplearning techniques and exceptional precision in detection. In medical image processing, convolutional neural networks are more commonly used as a deep learning approach and they are extremely effective.

III. EXPLANATION SYSTEM OF THE PROPOSED SYSTEM

3.1 NETWORK ARCHITECTURE

The fig 3.1 shows our proposed model for Alzheimer's Disease diagnosis. The first stage of the pipeline is the preprocessing. The second stage of the classifier is a deep convolutional neural network as shown in Fig. 3.2. The CNN model is a 2D network and follows a modified architectural pattern of ResNet50. The CNN classifier has several layers performing the convolution, batch normalization, rectified linear unit, and pooling operation. The layers follow a particular connection pattern known as dense connectivity. We keep these layers very narrow (e.g., 12 filters per layer) and connect each layer to every other layer. We will refer to the layers as dense layer and combination of the layers as dense block. Since all the dense layers are connected to each other, the fifth layer receives the feature-maps (h0, h1, h2, ..., hi−1), from all previous layers (0, 1, 2, ..., i−1). The network has aDeep CNN for Automated Diagnosis of AD and MCI Using 3D Brain MRI 7 global feature map set, where each layer adds a small set of feature-maps. Each layer can access the gradients from the loss function and the original input in training time. As a result, the flow of information improves, and gradient flow becomes stronger in the network. Final classification is performed by the softmax layer with three different output classes: Non-Dementia, Very Mild Dementia, Mild Dementia and Moderate. We optimized the CNN classifier using the Adam algorithm .

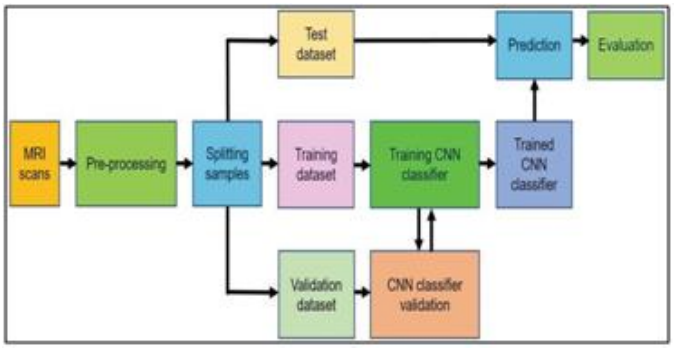


Fig 3.1 Block Diagram Of The Proposed Alzheimer's Disease Diagnosis Framework

3.2.1 CONVOLUTION LAYER

Convolutional layer is the base layer of CNN. It is responsible for determining the features of the pattern. In this layer, the input image is passed through a filter. The values resulting from filtering consist of the feature map. This layer applies some kernels that slide through the pattern to extract low- and high-level features in the pattern. The kernel is a 3x3

or 5x5 shaped matrix to be transformed with the input pattern matrix. Stride parameter is the number of steps tuned for shifting over input matrix. The output of convolutional layer can be given as:

$$x_j^l = f\left(\sum_{a=1}^{N} w_j^{l-1} * y_a^{l-1} + b_j^l\right)$$

wj here x^l is the j-th feature map in lajyer l, w^{l-1} indicates j-th kernels in layaer l-1, y^{l-1} represents the a-th feature map inj layer l-1, b^l indicates the bias of the j-th feature map in layer l, N is number of total features in layer l-1, and (*) represents vector convolutionprocess.

1.4 IMPLEMENTATION TOOLS

- Programming Language: Python
- Tools & Libraries: Google colab, sklearn and visualization libraries, Transfer learning pre-trained models, keras, tensor flow.
- IDE :GOOGLE COLAB
- Prerequisites: Python, Machine Learning, Deep Learning, Medical Image Processing.

1.5 STEPS FOR IMPLEMENTING THE MODEL

For Alzhemier Detection:

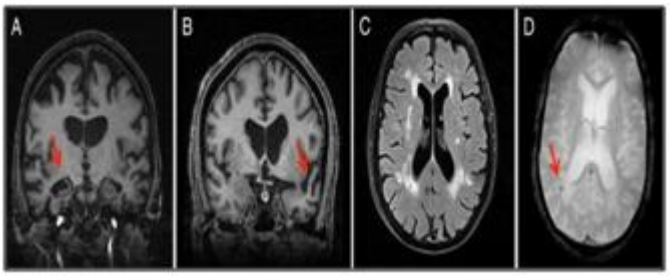


Fig 4.1 Image from

"POSTGRADUATE MEDICAL JOURNAL" of paper "BRAIN IMAGING IN DEMENTIA"

- The database provided a data set of 5121 training images with ratings.

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