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Analysis of MRI image data for Alzheimer disease detection using deep learning techniques

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Abstract
Alzheimer's disease (AD) is the leading cause of dementia globally and one of the most serious future healthcare issue. AD is expected to rise from 27 million to 106 million cases in the next four decades impacting one in every 85 people on the planet. For the existing healthcare systems, the most frequent kind of dementia is a significant source of worry. AD usually refers to Untreated Schizophrenia, a degenerative neurological disorder defined by memory loss and disorientation. AD is the world's third greatest cause of mortality, after only heart disease and cancer. It has surpassed cancer as the most dreaded disease on the planet. AD is catastrophic in the long-term run since it slowly but gradually destroys the body's cells. A variety of efforts have been made to employ structural Magnetic Resonance Imaging (MRI) modalities to differentiate between people with AD and their healthy counterparts. These have also been examined as deep learning algorithms for the categorization of MRI data. It is difficult to find patients with modest cognitive decline who may acquire Alzheimer's. As a result, creating deep learning-based disease detection techniques to assist clinicians in detecting prospective Alzheimer's patients is crucial. The performance comparison of the Imaging, Electronic Health Record (EHR), and Single Nucleotide Polymorphisms (SNP) datasets are evaluated using the metrics Accuracy, Sensitivity, Specificity, and Multi Area. Different mistakes are added under the curves for gradient calculation. The research results are as follows: based on standard datasets the results show that the proposed feature selection algorithms discover a sub-optimal minimal level feature set from a larger input feature set for diagnosing Alzheimer's disease, with higher values for system performance in terms of Accuracy as well as losses against training and Accuracy and losses against validation. These results can demonstrate the model's suitability for the purpose.

Keywords Deep learning (DL) · Cerebrospinal fluid (CSF) · Electronic health record (EHR) · Single nucleotide polymorphisms (SNPs) · Alzheimer's disease (AD)

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1 Introduction

Alzheimer's disease (AD) is among the most challenging diseases to cure. Alzheimer's disease is synonymous with senile dementia, a progressive mental and neurological decline. After stroke, cardiovascular disease, and cancer, Alzheimer's disease is the fourth leading cause of death worldwide. It has surpassed cancer as the most feared illness in the world. It kills more individuals than both breast and prostate cancers put together. Alzheimer's disease destroys the body over time until death occurs. At least 50 million people worldwide were living with Alzheimer's in 2018. The World Health Organization (WHO) reports that 4-8% of adults over 65 have dementia. The risk of developing Alzheimer's disease increases to 35% after the age of 85 [12, 16, 29]. The current pathophysiology of Alzheimer's disease is uncertain. The loss or destruction of synapses and axons is widely believed to be related to the buildup of Amyloid- (A) in intracellular and Neurofibrillary Strands [27, 33]. The transition from old age to Alzheimer's disease causes the early onset symptom known as mild cognitive impairment (MCI). MCI is commonly misdiagnosed as being the result of normal aging. Fourty-four percent of people diagnosed with MCI subsequently acquired Alzheimer's disease [4]. Patients with MCI can improve their quality of life with the help of psychotherapies and medications. Research into Alzheimer's disease is currently the field's top priority. At least $100 billion dollars is spent annually on Alzheimer's research and care.

1.1 Deep learning

A multi-layer computational paradigm, Deep Learning (DL), for data representation on many abstract levels [19]. Despite the fact that deep learning had tremendous progress in the computer field, identifying and classifying medical pictures remains a serious difficulty. It has advanced considerably in the interpretation of medical pictures in recent years. Deep learning method for distinguishing between MCI and Cognitively Normal (CN), AD and MCI, AD and CN. Accuracy levels are 95.9 % (AD versus CN), 75.8 % (MCI versus AD), and 85.0 % (CN versus MCI) [24]. The features below are removed from "Positron Emission Tomography" and "Magnetic Resonance Imaging" images using a comprehensive Boltzmann machine, while the "Support Vector Machine" process is used for final categorization. But there is a procedure that simply employs four-layer networks, which makes it complicated to separate abstract image features.

Convolutional Neural Network (CNN) is considered a great artificial neural network feed-forward class [5, 8]. Image identification and classification are the two most essential applications of deep learning. It is directly utilizing the two-dimensional pictures as data entry and then learns automatically from the data that the conventional (conv) hand-held extraction functions produce to prevent various calculation mistakes. It can extract better characteristics to describe the delicate lesion locations [5, 8, 24]. It is utilized to distinguish between normal, healthy human brains and Alzheimer's disease [22]. It uses CNN for AD brains with an accuracy rate of 96.86% in a healthy person's brain [7, 25]. Using networked LeNet-5 and networks, images from "Structural Magnetic Resonance Imaging" (SMRI) and "Functional Magnetic Resonance Imaging" (FMRI) are integrated and used to classify Alzheimer's disease. While more accuracy

should be achieved by only healthy ageing people and Alzheimer's patients are recognized, the procedure is not utilized in "Magnetic Resonance Imaging". In Eq. 1, the error is computed at the backpropagation stage.

$$\frac{\partial E}{\partial W_{ab}} = \sum_{i=0}^{N-m} \sum_{j=0}^{N-m} \frac{\partial E}{\partial W_{ij}^{l}} \frac{\partial x_{ij}^{l}}{\partial W_{ab}} \tag{1}$$

$$= \sum_{i=0}^{N\text{-}m} \sum_{j=0}^{N\text{-}m} \frac{\partial E}{\partial W_{ij}^{l}} y_{(i+a)(j+b)}^{l-1} \tag{2}$$

Where E is the error function, x is the input, y is the i^{th}, j^{th}, m is the filter size, N is the number of neurons in each layer, l is the layer number, and w is the filter weight with a and b indices, and N is the number of neurons in each layer. Figure 1 shows the Progress of Alzheimer's Disease. The left side of the image shows healthy human brain which don't have any enlarged ventricles whereas the right side shows the Alzheimer's effected brain which consists of enlarged human ventricles causing progressive degeneration of brain cells [3].

In this paper we have discussed and found out various research methodologies for early detection of alzheimer's disease and have used EHR and SNP dataset.These data sets are used as an input in various deep neural network frameworks.The datasets are discussed in the following section. Convolution neural network has been used to analyze the MRI images.After deriving the confusion matrix the model's accuracy,precision,recall F1score has been calculated and compared using various deep learning frameworks like CNN,DENSENET,RESNET50 and VGG.It has been

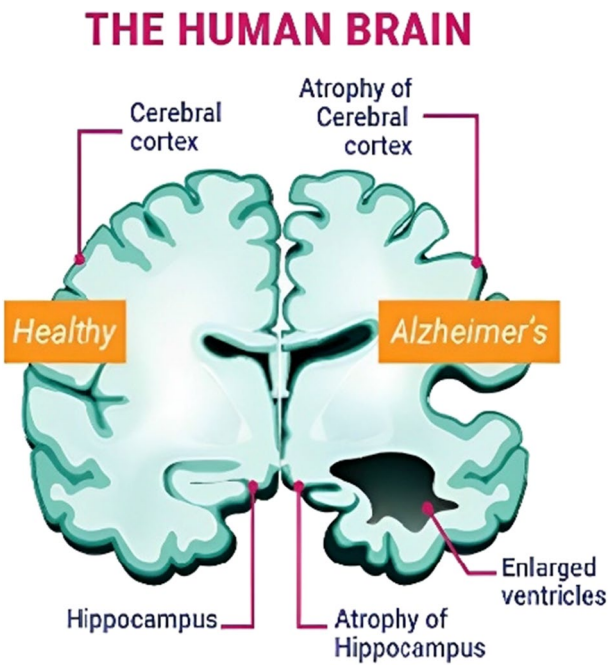


Fig. 1 Progress of Alzheimer's Disease [25]

found accuracy rate is highest using SNP datasets ,hence giving clarity on the detection and classification of Alzheimer's Disease.

2 Review of literature

In this section, we have discussed the research content by the researchers. Janani et al. [30] investigated the single data modes utilized to forecast the stages of Alzheimer's disease (AD). The integration of many data modalities yields a comprehensive picture of AD Stage Analysis. As a result, it makes substantial use of Deep Learning (DL) to evaluate imaging, magnetic resonance imaging, and diagnostic trials for Alzheimer's disease, genetics (SNPs), MCI, and control. It is used to stack noise removal drivers to obtain parameters from imaging data and clinical and genomic. In addition, it provides a novel method for data interpretation to identify high-performance features generated from deep models through clustering and disturbance analysis. These results are being used to illustrate those deep models are much better than shallow models (such as decision trees) in rating, particularly when it comes to search results and relevance. K-nearest neighbours, random forests, support vector machines, and decision trees are just a few examples. Furthermore, it demonstrates that combining multimodality data yields more accurate, exact, recoverable, and medium F1 scores than single modality models. The hippocampus or amygdala mind regions and "Rey Auditory Verbal Learning Test" (RAVLT) as the highest characteristics that conform to known AD literature.

Ebrahimighahnavieh et al. [10] state that Alzheimer's Disease is a leading reason of death in technologically advanced countries. Although the research results were excellent, no clinically effective diagnostic techniques based on computer-aided algorithms were available. Deep models have been more popular in recent years, especially in the realm of photography. Deep learning is an extra accurate and traditional machine learning technique in detecting Alzheimer's disease. However, identifying Alzheimer's disease remains challenging or necessitates a highly discriminating representation of the features to differentiate similar brain patterns for classification. It offers the developments and findings based on a thorough review of over 100 articles. It focuses on critical biomarkers, pre-processing processes, and various approaches to data management in single-mode and multimodal research.

Mehmood et al. [21] stated that AD irreversibly affects memory cells, eventually leading to dementia. Alzheimer's disease prevention activities are a complicated issue for researchers to tackle. Classification algorithms and strategies based on Coevolutionary Classification Network (CNN) are readily accessible for addressing a range of challenges associated with this form of data processing. Magnetic resonance scanning is used to identify Alzheimer's Disease (AD) in clinical studies. They intend to extract highly discriminative features from Magnetic Resonance Imaging scans in order to properly categorize dementia stages. Recent advances in the accuracy of deep convolution neural models have shown their use. Furthermore, because the datasets contain a small number of image samples, over-fitting concerns arise, impairing the performance of deep learning models. To diagnose dementia phases, the researchers designed a Symmetrical Convolution Network (SCNN) architecture inspired by VGG-16 (a.k.a. Oxford Net). They complement the sparse and imbalanced data in our strategy by applying augmentation techniques. The open-access series of imaging tests dataset was used in the investigation. The proposed technique achieves a critical overall accuracy of 99.05 per cent for dementia stage categorization.

According to Zhang et al. [34], Alzheimer's disease is one of the most difficult disorders to treat. Alzheimer's disease has a significant impact on the elderly and their family. MCI is the transition between normal ageing Alzheimer's and AD. The appropriate therapy is

missed MCI is frequently misinterpreted as a sign of normal ageing. MCI is essential for Alzheimer's disease diagnosis and treatment. This article presents a comprehensive pattern for the auxiliary diagnosis of Alzheimer's disease that closely resembles a physician's diagnostic approach. Neuroimaging and cognitive diagnostic tests are often used to identify people who may have Alzheimer's disease. In this study, two separate neural convolutional networks train multimodal medical pictures. The output stability of two deep neural networks is then determined using correlation analysis.

Ji et al. [14] state that Alzheimer's disease leads to further impairment and memory loss. It has a significant impact on patients' lives and is not curable. The detection of Alzheimer's disease is helping to initiate proper treatment to avoid further brain damage. Alzheimer's disease classification has been subjected to machine learning methods over the past few decades, with outcomes based on physically generated characteristics and crosses architectural classifiers for pattern categorization. The end-to-end approach of neural networks was employed in conjunction with deep learning. The main goal of this study is to develop a technique based on CNN for detecting Alzheimer's disease in its early stages using Magnetic Resonance Imaging. Grey and white matter image As categorization inputs, Magnetic Resonance Imaging slices were used. Ensemble learning processes collaborative learning processes were utilized to enhance classification by combining deep classification findings.

Tyagi, A., et al. [28] CAD can diagnose schizophrenia early using neuroimaging modalities due to its repeatability. Schizophrenia causes brain structural abnormalities and delusions. sMRI can detect brain structural abnormalities. Machine Learning (ML) can be used to identify categorization biomarkers and help diagnose schizophrenia. This research offers an ML-based schizophrenia diagnosis algorithm on 146 structural MRI datasets. We used Support Vector Machine, Logistic Regression, Decision Tree, k-Nearest Neighbour, and Random Forest to categorise schizophrenia and healthy control. Image selection, conversion, grey scale, and flattening were used to pre-process structural MRI scans. We also tested the model using hold-out and stratified 10-fold cross-validation. SVM accuracy was high after stratified 10-fold cross-validation. Using hold-out validation to evaluate the classifier, k-Nearest Neighbour fared better.

Martinez-Murcia et al. [20] studied that several conventional machines have been applied to Alzheimer's disease, including image decomposition segmentation methods such as major component analysis to greater complexities and nonlinear decomposition algorithms. Deep learning is based on abstract high-level properties extracted from Magnetic Resonance Imaging scans that determine how data is distributed internally to low-dimensional manifolds. There is attempting a new Alzheimer's disease experimental data analysis based on deep learning in this investigation. By integrating information regarding neuropsychological test results, and clinical data along with pictures obtained only by data-driven degradation of Magnetic Resonance Imaging. It is expected to uncover links between the process of neurodegeneration and cognitive disorders. The impact of each automatic coordinate on the brain is then evaluated by examining various combinations of the features. This is accomplished via the use of regression and gradation analysis. Clinical variable quantity with associations over 0.6 in the case of neuropsychological assessment measures such as Mini-Mental State Exam (MMSE) or Advanced Driver-Assistance Systems (ADAS11), reaching a classification precision of more than 80% used for the Alzheimer's disease diagnosed.

Allioui et al. [2] stated that Learning techniques are crucial for finding previously undetected brain diseases. In learning-based systems, MRI is utilized to reconstruct a solution for detecting abnormal values or locations in the neural network. The focus of the research

is to present a technique for autonomously segregating the brain's ability to diagnose Alzheimer's disease and identify brain damage (AD). They offer a 2.5D approach for detecting and categorizing brain inflammation that makes use of the benefits of 3D with minimizing complexity and computational expenses. Our proposed approach is evaluated using data that is publicly available. Preliminary findings indicate that Alzheimer's Disease Detection Method is both trustworthy and effective and, therefore, that their technology advances the existing understanding of Alzheimer's disease diagnosis.

Aderghal et al. [1] introduced a new imaging method, and Diffusion Tensor Imaging complements structural Magnetic Resonance Imaging in Alzheimer's disease research. A recent study has concentrated on pathologic grading of Alzheimer's disease utilizing Diffusion Tensor Imaging Mean Diffusivity maps. Deep Neural are alluring devices for comuter-assisted Alzheimer's disease therapy. The primary challenge is a scarcity of publicly accessible training data with both modalities. Inadequate training data results in overfitting. Cross-modal transfer learning by Diffusion Tensor Imaging with structural Magnetic Resonance Imaging. Retraining on Mean Diffusivity information is performed using pre-trained models on structural Magnetic resonance dataset with domain-dependent data augmentation. The strategy reduces over-fitting, enhances learning performance, and hence boosts prediction accuracy. These scores are then significantly improved in a subset of the ADNI dataset by a clear majority of Normal Controls, Alzheimer's Patients, or Mild Cognitive Impairment persons.

Alzheimer's disease is a neurodegenerative disease that damages the brain, according to Islam et al. [13]. It wreaks havoc on brain cells, weakening people's memory, cognitive capacities, and ability to perform simple activities.

While Alzheimer's Disease could be cured, early detection and treatment can dramatically alleviate symptoms. Machine learning algorithms offer the potential to speed up the diagnosis of Alzheimer's disease. Recent research has demonstrated that deep learning models are extremely effective in analyzing medical images. However, it looks as though there is a shortage of research about the use of neural net approaches to Alzheimer's disease diagnosis. The researchers created a unique deep learning technique for detecting and diagnosing Alzheimer's disease using magnetic resonance data. They create a very detailed CNN model and test its effectiveness using the OASIS database.

Verma et al. [31] studied that doctors and radiologists can use CAD systems to detect disease. Deep learning CAD systems can diagnose brain tumours, but they are computationally intensive and difficult to deploy in real-time situations that require speed and precision. As brain-tumor classification includes modelling pixel-to-pixel relationships and spatial-contexts in tumor-affected regions, deep-learning algorithms must collect multi-scale information. To classify brain tumours, this study introduces deep, efficient, and lightweight deep learning architectures with innovative weight initialization and layers freezing for representational feature learning. Four transfer learning weight initialization and freezing setups and one random initialization are used. These setups use alternative parameters and memory-efficient designs. Performance is optimal when architecture is begun properly with weight initialization configuration based on trainable parameters and architectural depth. 40 deep learning frameworks were trained and evaluated using eight CNN architectures and five weight initialization setups. From the comprehensive experimental analyses of classification performances over three classes of brain tumour, DenseNet201 based transfer learning model with initial 5 convolution layers frozen achieves state-of-the-art accuracy of 98.22% while the lightweight models of MobileNet outperform many other models with the highest 97.87% accuracy for transfer learning configuration with initial 3 convolutional layers frozen while sizing

only 42.6 MBs. DenseNet201 uses densely-flowing skip connections to learn features from multiple spatial contexts and analyse them in line with current receptive fields. The 5 convolutional layer frozen transfer-learning approach outperforms state-of-the-art algorithms by 0.88%. The random initialization paradigm's efficacy for brain tumour classification is also examined. If the number of trainable parameters matches training data quantities, the framework may be promising.

Ortiz et al. [23] suggested that Computer-aided diagnosis (CAD) enables earlier and more effective therapy choices for Alzheimer's Disease (AD). The purpose of this research is to see if neural network models can be used to classify brain areas discovered via Autonomous Anatomical Localization (AAL). Grey matter pictures were separated into three-dimensional patches suitable for spanning numerous deep belief networks using the AAL atlas. The ultimate forecast is made by a vote on a machine learning aggregation.

Three architectures based on deep learning and four voting methods were constructed and evaluated to develop a robust categorization architecture.

A large dataset from the Alzheimer's Disease Neuroimaging Program was used to validate the approach. Cross-validation findings demonstrate that the suggested technique is successful not only at discriminating among NC and AD pictures but also at recognizing faces with Neurological Dysfunction. It gets a classifier performance of 0.90 as well as an AUC of 0.96 with steady MCI/AD conversions. Table 1 shows the summary table for the Literature review. The table summarizes latest methodologies about extraction of features from clinical and genomic data,finding out the ROI,design of SCNN model,deep learning methods to train the model and ensemble classifier.

A new Alzheimer's disease screening approach was discovered using deep convolutional neural networks. To make an early diagnosis of this disease, it is imperative to do a clinical assessment of the patient's cognitive testing, medical history other pathological assessments. Along with these clinical tests, there are a variety of different approaches for diagnosing Alzheimer's disease, including cerebrospinal (CSF) analysis, biomarker analysis, brain scans (MRI/PET), and plasma proteins analysis. To help in diagnosis, a discrete wavelet transformation (DWT) approach was utilized to produce feature wavelets for Alzheimer's disease categorization. This does not provide disease identification; extra processing is necessary using machine learning algorithms.

As with machine learning approaches, hand-crafted feature extraction methods involve considerable work to construct the features. When compared to traditional techniques of feature learning, such as machine learning, supervised learning methodologies, such as deep learning frameworks, are smart enough to learn higher-level features from datasets. The Spyder program from the anaconda distribution is used to model Deep Convolutional Neural Networks (DCNN), together with the Kera library and Convolutional backend on GPU. When the Alzheimer's Disease Neuroimaging Initiatives (ADNI) dataset is used, the results show an accuracy of 98.57 per cent. The datasets were utilized to optimize using various optimizers, and the results were compared to determine which optimizer was better [31].

The research objectives of this paper are as follows:

- To get data for all three points (imaging, EHR, and SNP) from publicly available sources.
- To generate a Deep Convolutional Neural Network (DNCC) for individual modality. The DNCC is used with Integral analysis for all three datasets.
- To validate and optimize the system using the gradient computation method.
- To detect the errors between actual and generated results.

Table 1 Literature review summary table

S. No.	Authors	Approach/Methodology	Conclusion
1	Janani et al. (2021), [30]	Extract characteristics from clinical and genomic data using stacked denoising auto-encoders	The hippocampus, amygdala, and the Rey Audiovisual Verbal Learning Task (RAVLT) were found as the most distinguishing traits.
2	Ebrahimighahnavieh et al. (2020), [10]	Methods that rely on regions of interest (ROI) and patches	CNNs have been utilized the most frequently and have exhibited higher accuracy in this domain than other deep models.
3	Mehmood et al. (2020), [21]	SCNN model is inspired by the Siamese fully convolutional (VGG-16).	The categorization of dementia phases is performed with a high degree of accuracy, 99.05 per cent.
4	Zhang et al. (2019), [34]	Deep learning trains the multimodal auxiliary diagnostic model.	Better performance and the ability to get a good diagnosis of AD in the auxiliary tests.
5	Ji et al. (2019), [14]	ConvNet-based ensemble classifier.	The classifications have an accuracy rate of up to 97.65 percent in the case of AD/mild cognitive impairment and 88.37 percent in the case of mild cognitive impairment/normal control.
6	Martinez-Murcia et al. (2019), [20]	Machine learning for feature extraction using partial least squares	elucidate regional brain structural disparities between persons with autism and normally evolving individuals
7	Allioui et al. (2019), [2]	CAD system segmenting 2.5D pictures to assess brain damage and Alzheimer's illness	This strategy enables us to attain a 92.71 percent accuracy rate, a 94.43 percent sensitivity rate, and a 91.59 percent specificity rate.
8	Aderghal at al. (2018), [1]	Using DTI-MD & sMRI brain signals, a classification strategy based on cross-modal domain adaptation is offered for AD diagnosis.	demonstrates a reduction in over-fitting, improves learning efficiency, and hence boosts accuracy rate
9	Islam et al. (2017), [13]	The OASIS database's deep convolutional network.	delivered a single-step analysis of brain Magnetic Resonance Imaging data with the purpose of detecting and classifying Alzheimer's disease
10	Ortiz et al. (2016), [23]	Automated Anatomical Labeling via Deep Learning	When compared to the harder case of identifying Mild Cognitive Impairments (MCI) Subjects, performs brilliantly.

2.1 Challenges

Alzheimer's, an irreparable brain disease, impairs thinking and memory while mind size shrinks, which is at last prompt disease. Early detection of Alzheimer's disease (AD) is critical for the advancement of more effective treatment. In the domain of computer vision, machine learning, which uses deep learning to discover subtle structures in complex high-dimensional data, has beaten traditional automation. Deep convolutional neural networks have sparked renewed interest in the early diagnosis and characterization of Alzheimer's disease. Rapid advances in neuroimaging techniques have resulted in the collection of enormous amounts of different neuroimaging data. The majority of current AD and moderate cognitive dysfunction (MCI) research makes predictions using a single data modality, such as the AD stage. When different data modalities are combined, it is possible to achieve a comprehensive analysis of the staging of AD. Thus, in the current work, we have applied deep learning over the individual data modalities and also to integrally analyze genetically (single nucleotide polymorphisms (SNPs)), imaging (Magnetic Resonance Imaging) and clinical test results are used to categorize patients into stages of Alzheimer's disease. In the current work of individual modalities, Deep Convolutional Neural Network (DCNN) is used with the integral analysis of all three data modalities using concatenation. The validation and optimization of the outcomes are served using gradient computation for error rate detection between actual and generated.

3 Research methodology

In the proposed methodology, there are three datasets taken imaging dataset, EHR dataset and SNP dataset. Each datasets are discussed below in detail in the following section:

3.1 Imaging dataset

Imaging data sets are utilized in several approaches to exercise and/or test algorithms. Although many large datasets used to teach CNN for image identification involve hundreds of images, smaller data sets are adequate for texture classification, learning techniques, and other applications. The proposed model employs preprocessing approaches for training and testing medical images. Magnetic Resonance Imaging images degrade during the production process due to low variation induced by the optical equipment's weak brightness. To solve this problem and optimize Magnetic Resonance Imaging scans, image processing methods, including linear contrast enhancement, were utilized to increase pixel dispersion across a broad range of brightness levels [23, 32].

3.2 EHR dataset

Whether there is an electronic health record (EHR) or a clinical database, the goal is the same to help patients lead healthier lives. A patient's electronic chart is a carbon copy of his or her paper chart. Electronic Health Records (EHRs) are patient-centric, real-time records that allow authorized users to swiftly and securely access relevant information. While an EHR system retains a diagnosis, it is also meant to go beyond standard clinical data acquired in a provider's office to provide a more holistic view of a patient's treatment [18]. For the electronic health record to be successful, there are three key characteristics: First, the electronic

health record empowers authorized physicians to build and maintain health records in a digital format that is accessible to specific other clinicians across multiple health care organizations. A patient's EHR is intended to offer information to healthcare practitioners as well as a variety of other health care providers and institutions, including pharmaceuticals, doctors, diagnostic centres, dispensaries, emergency care, and college and occupational clinics.

3.3 SNP dataset

The human genome is made up of around three billion nucleotides (DNA base pair) pairs. Only 1% of them differ across people, and nearly the majority of them are the same among all humans (population). Single Nucleotide Polymorphisms (SNPs) account for a major fraction of these genetic variants. SNPs have been linked to a variety of biological impacts, including the relationship with complicated disorders and diverse reactions to drugs and therapies, according to research. It also has several advantages over microarray gene expressions, such as being less likely to change over time. That is, a patient's SNPs at birth will remain the same throughout his or her life [6]. A huge number of genetic variants are currently being identified and evaluated. The method calls for three stages. Data preparation is the first phase; feature extraction from input visuals is the second stage; and the last stage is automatic decision making with Convolution layers, max-pooling levels, and batch normalization layers, three layers of the algorithm performed concurrently. The classification accuracy was enhanced by using multiple parallel layers in a row. All the steps are as follows:

- In the first stage, data from the various datasets will take for evaluation. All three datasets are easily accessible. There are numerous of data available about patients with AD. This information can be used to identify the different initial symptoms and the time of starting the disease.
- The second phase involves the preprocessing of data and the extraction of features related to AD. They must be transformed into the appropriate format (JPG, PNG, TIFF, etc.) after being acquired in order to be used for further processing [9].
- In the third stage, three layers of work method work parallelly so that the accuracy of the system will improve and the best outcomes can be achieved. In this step, three batch normalization layers, five max-pooling levels, and 14 Convolution layers, three layers of the algorithm, are performed concurrently for best performance. After that outcome of each group is concentrated for further optimization process so that the best results will be found. The optimization is performed using an integral analyzer, and gradient computing is also used for error detection. The suggested methodology's workflow model is depicted in Fig. 2.

3.4 CNN

CNN, also known as Convolution Network, is a type of Artificial Neural Network (ANN) with deep feed-forward architecture and tremendous simplification capabilities when combined with several networks having fully connected (FC) layers.

Figure 3 depicts CNN's core conceptual paradigm [10]. This is capable of comprehending and detecting highly conceived elements of stuff, particularly spatial data. The figure shows a deep CNN model is made up of a limited number of processing layers which can learn numerous levels of abstraction from input images. The initiatory layers learn and extract higher-level qualities (with less abstraction), whereas the deeper layers learn and extract lower-level traits [10].

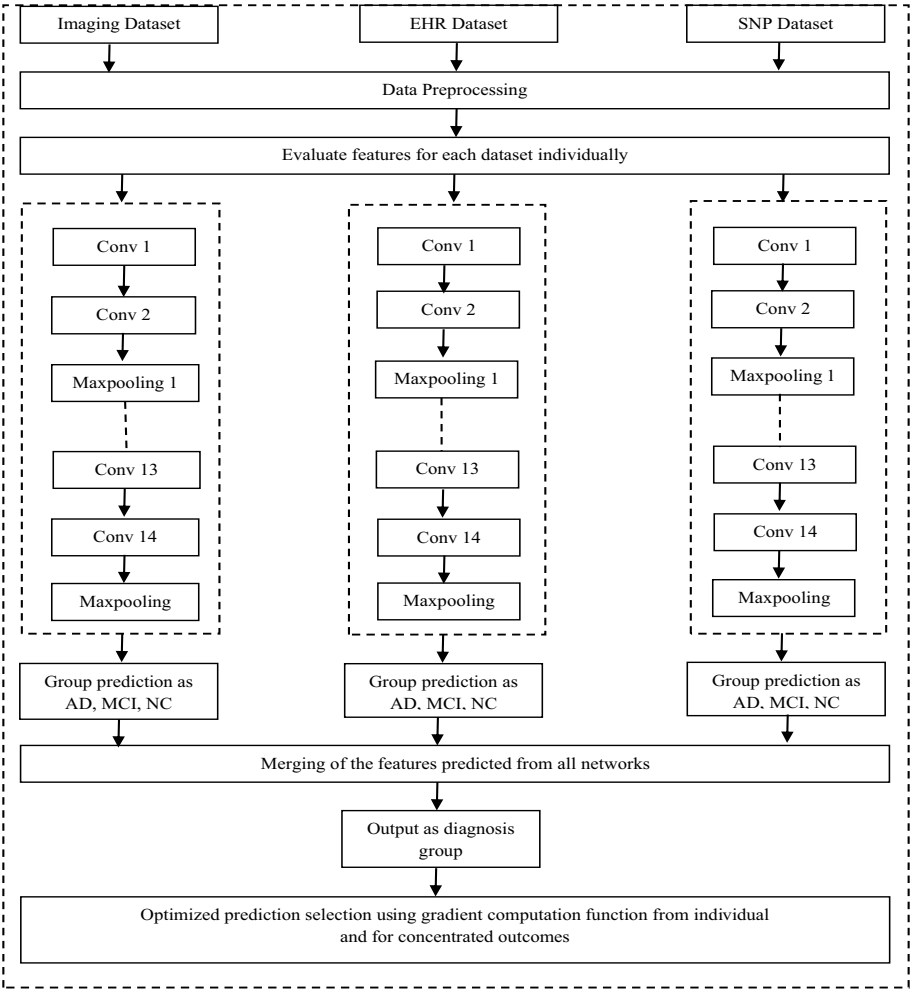


Fig. 2 Proposed architecture for AD stage detection

The input image is fed intro the convolutions layers which applies filter to the input image which helps to filter out only certain informations from the image.Inorder to retrieve more refined information the output of each convolution layer is passed through convolution 2 and convolution 3 layer to get exact refined information.The final output image from convolution 3 layer is fed into the fully connected layer which performs the mathematical operations of classification and finally passed through dropout layer to reduce overfitting .

At the time of examining the feature maps generated by the convolution layers, it is seen that they are very dependent on the placement of the features in the input. This problem can be overcome by down-sampling the extracted features. Therefore, in order to strike a balance between processing resources and the extraction of significant characteristics, downsizing or down-sampling should occur at appropriate intervals.

This is accomplished using a concept known as max pooling. Pooling is a technique for down-sampling feature maps by enumerating the features present in the feature map.

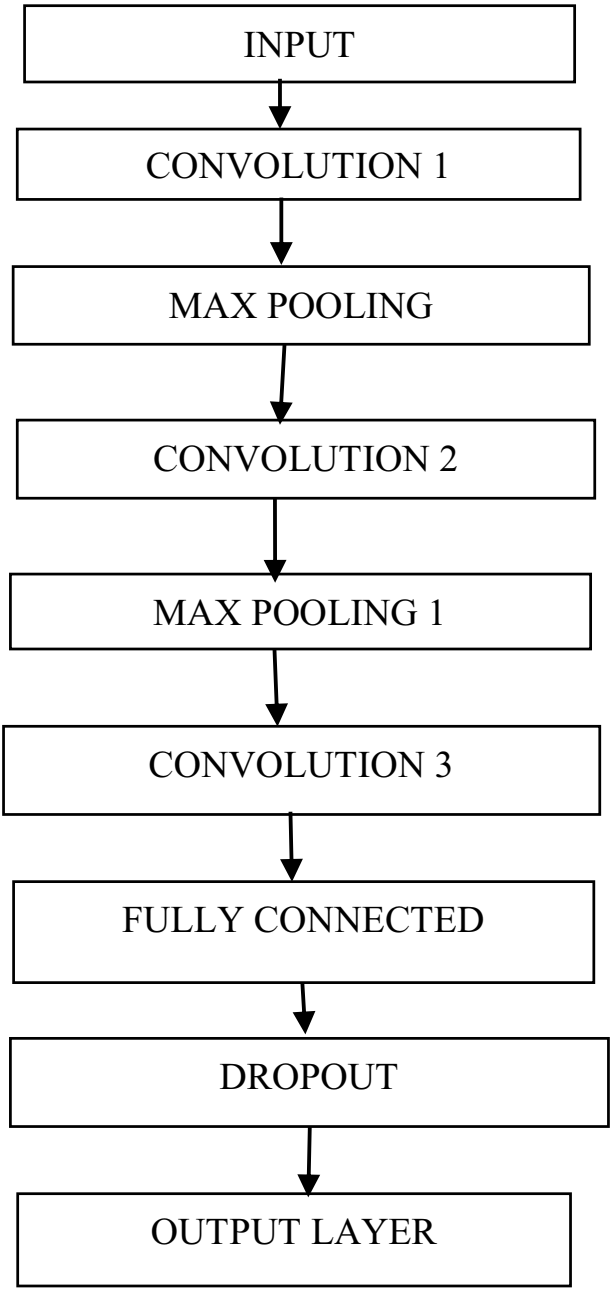


Fig. 3 CNN Architecture [10]

Dropout is a method for optimizing neural networks by minimizing overfitting. The primary objective is to prevent hidden units from co-adapting. Dropout boosts neural net performance in a wide variety of application domains [21].

4 Implementation tool used

The suggested method utilizes three datasets, an imaging dataset, an electronic health record dataset, and a genetic variation dataset. Python is used for the actual implementation of the study technique [34]. The implementation also made use of Confusion Matrix which allows for more precise model predictions.

4.1 Confusion matrix

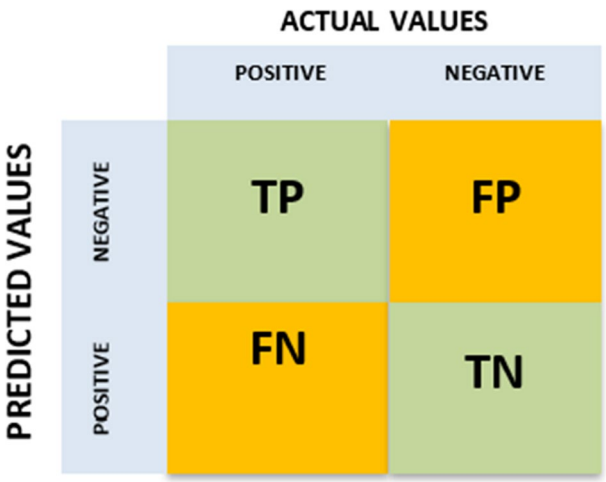
The matrix is N x N. It's used to evaluate the effectiveness of a classification model, where 'N' stands for a number of target groups. The matrix relates real objective values to machine learning model predictions. For a binary classification query, a 2 x 2 matrix with four values is used to gain a detailed view of how well our classification model is performing and to calculate the accuracy using these actual and projected values which is shown in Fig. 4. The objective variable's actual values are displayed in columns. The anticipated values of the goal variable are shown in rows. The target variable has 2 values: positive or negative. Figure 4 shows the Confusion Matrix [14].

In this confusion matrix, there are four parameters which are as follows:

4.1.1 True positive (TP)

- The real value and the expected value are similar.
- The true value is positive, as is the model's anticipated value

Fig. 4 Values Matrix



4.1.2 True negative (TN)

- The real value is negative, and the model's predicted value is also negative.
- The anticipated and actual values are very comparable.

4.1.3 False positive (FP) – Type 1 error

- Type 1 error is another name for it.
- Although the actual value is negative, the model's predicted value is most likely positive.
- The value predicted for the prediction was inaccurate.

4.1.4 False negative (FN) – Type 2 error

- A Type 2 mistake is another name for this.
- The anticipated value is mistakenly expected.
- Although the true value is positive, the model's predicted value is negative.

The values of the confusion matrix can be used to calculate the following value: In the proposed methodology, there are three datasets taken imaging dataset, EHR dataset and SNP dataset. These are discussed below. The implementation of the research methodology is done over Python [14]. Additionally, Confusion Matrix was employed in the implementation. It is used to forecast the model's accuracy.

The model's accuracy
The model's accuracy can be assessed as follows:

$$\text{Accuracy} = \text{TP} + \text{TN}/\text{TP} + \text{FP} + \text{TN} + \text{FN} \tag{3}$$

The model's precision
The model's precision can be measured as follows:

$$\text{Precision} = \text{TP}/\text{TP} + \text{FP} \tag{4}$$

Model Identification
The recall of the model can be calculated as:

$$\text{Recall} = \text{TP}/\text{TP} + \text{FN} \tag{5}$$

Where TP= True positive, FP= False Positive, TN= True Negative, FN= False Negative.

5 F1 score of models

The F1 score is then calculated by:

$$2 * \text{precision} * \text{Recall}/\text{precision} + \text{Recall} \tag{6}$$

6 Result discussion

This section compares the outcomes of the suggested approach to the research findings [26].

6.1 Result I: (Imaging dataset)

This section displays the results of the training Dataset. The accuracy of train data received is 95.448 per cent. The results of the imaging dataset for the Moderate Demented, Mild Demented, and Non-Demented Classes are shown in Fig. 5.

The imaging dataset is shown in Table 2. Table 2 shows the Precision, Recall, F1-score, and support value for Non-Demented, Very Mild Demented, Mild Demented, Moderate Demented, Micro average, Macro average, Weighted average, and Sample average for Non-Demented, Very Mild Demented, Mild Demented, Moderate Demented, Micro average. This section displays the training Dataset results. The accuracy of train data is 95.448 per cent.

Figure 6 shows Alzheimer's Disease Diagnosis matrix representing Actual value vs predicted and it is also representing in rows and columns four classes of Alzheimer Disease, Non-Demented, Very Mild Demented, Mild Demented and Moderate Demented. The values represent the micro average ,macro average ,weighted average and sample average which is obtained from precision ,recall and f1 score metrics as explained in the above table (Table 2). These are scoring metrics for multiclass classification in machine learning.

6.2 Result II: (EHR dataset)

The results for EHR Dataset are shown in this section. The accuracy that is received by this model is 93.617%.

The Confusion Matrix of the test dataset is:

$$\begin{bmatrix} 40 & 4 \\ 2 & 48 \end{bmatrix}$$

Figure 7 depicts the graph of train loss for the EHR dataset and shows that increasing epoch values reduces the loss; when the value of epoch crosses 80, the loss gives a value less than 0.050.

Figure 8 depicts the graph of Validation loss for the EHR dataset and shows that increasing epoch values reduces the loss.

Figure 9 demonstrates the gradient computation for no. of iterations for the EHR dataset. With the help of this, the value of the Mean square error from gradient descent prediction is found to be 0.362.

Table 3 shows the Mean Absolute Error value is 0.09702000299436321, the Mean Squared Error value is 0.04618280907367353, Root Mean Squared Error value is 0.019978897434111005.

6.3 Result III: SNP dataset

The results for SNP Dataset are shown in this section. The accuracy that is received by this model is 99.2%. The Confusion Matrix of the test dataset is as follows:

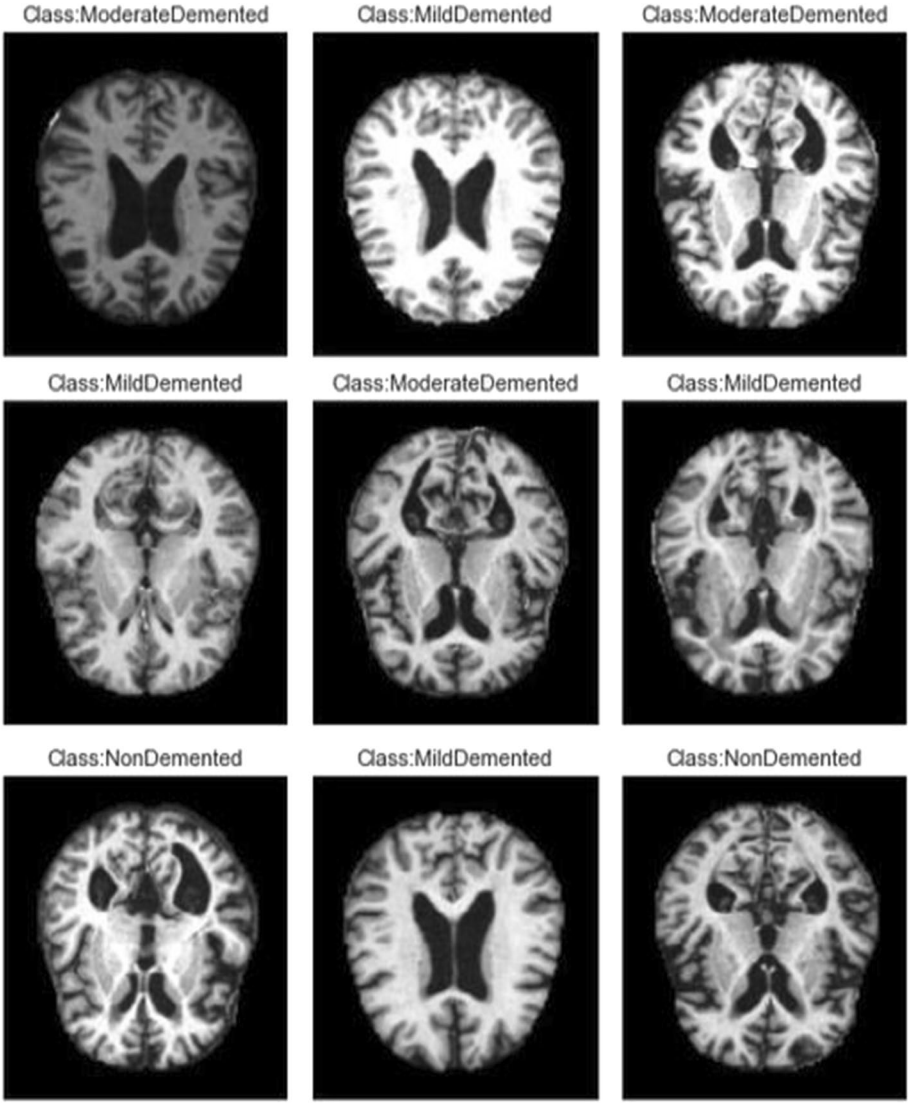


Fig. 5 Imaging dataset

Table 2 Important Parameters

	Precision	Recall	F1-score	Support
Non-Demented	0.69	0.64	0.66	201
Very Mild Demented	0.50	0.17	0.25	6
Mild Demented	0.90	0.27	0.42	643
Moderate Demented	0.42	0.90	0.58	430
Micro avg	0.54	0.54	0.54	1280
Macro avg	0.64	0.49	0.48	1280
Weighted avg	0.74	0.54	0.51	1280
Samples avg	0.54	0.54	0.54	1280

ACTUAL VALUE	NonDemented	128	0	0	73
	VeryMildDemented	5	1	0	0
	MildDemented	17	1	173	452
	ModerateDemented	35	0	7	388
		NonDemented	VeryMildDemented	MildDemented	ModerateDemented
	PREDICTED VALUE				

Fig. 6 Alzheimer's Disease Diagnosis matrix

Fig. 7 Training loss

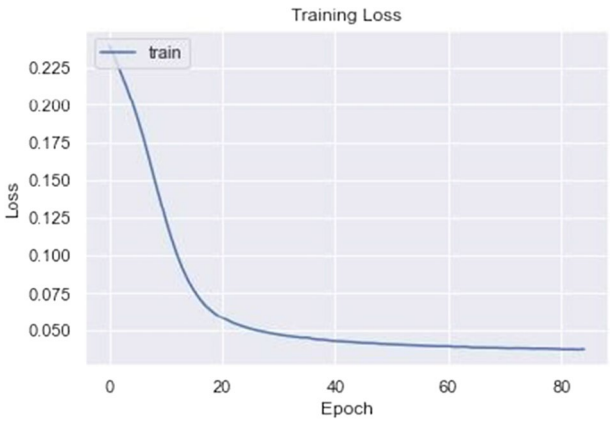


Fig. 8 Validation loss

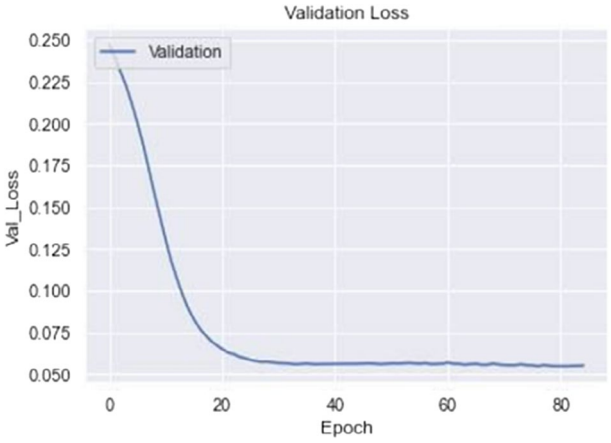
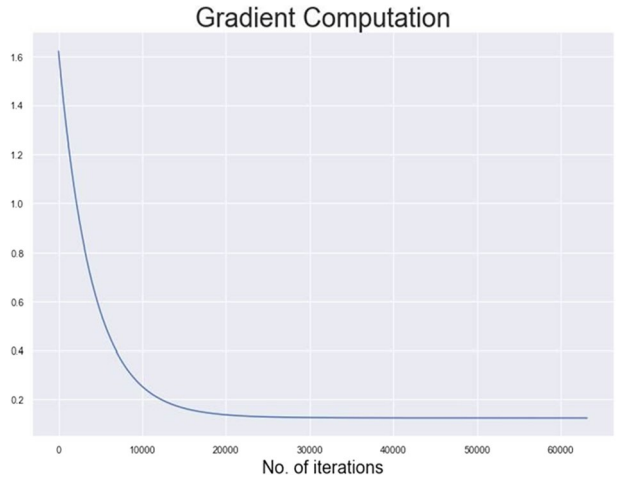


Fig. 9 Gradient computation



$$\begin{bmatrix} [61 & 0 \\ 1 & 63] \end{bmatrix}$$

Figure 10 demonstrates the graph of train loss with respect to epoch value for SNP Dataset.

Figure 11 demonstrates the graph of Validation loss with respect to epoch value for SNP Dataset.

Figure 12 illustrates the Gradient Computation graph for the SNP dataset. It demonstrates the gradient computation across the number of iterations for the SNP Dataset. When the number of iterations surpasses 6000, the gradient computation value is lowered to 0.2.

The value of the mean square error for decent gradient prediction is 0.247 because of using this method. With the use of this model, the mean absolute error is 0.25433, the Mean Squared Error is 0.137049, and the Root Mean Squared Error is 0.11706. Table 4 shows the error values of the model.

The comparison of the results to previous work is shown in Table 5. According to the analysis, It is concluded that the suggested strategy outperforms the other methods. These findings support the accuracy of the proposed technique for detecting Alzheimer's disease is better than the existing work in [1, 15, (Link 1: https://www.healthit.gov/faq/what-electronic-health-record-ehr)].

7 Implementation using various deep learning frameworks

There are other deep learning frameworks like DENSENET,RESTNET50,EFFICIENTNET and VGG.Here we are implementing all these models to test the datasets. Mainly for four classes of Alzheimer Disease, Non-Demented, Very Mild Demented, Mild Demented and

Table 3 Error-values of the model

Mean Absolute Error	0.09702
Mean Squared Error	0.055232
Root Mean Squared Error	0.235014

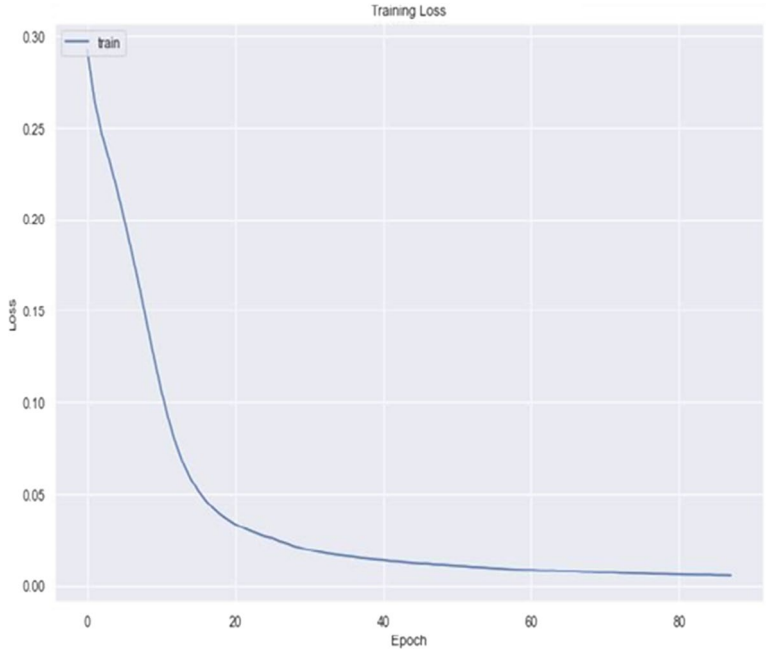


Fig. 10 Training Loss for SNP Dataset

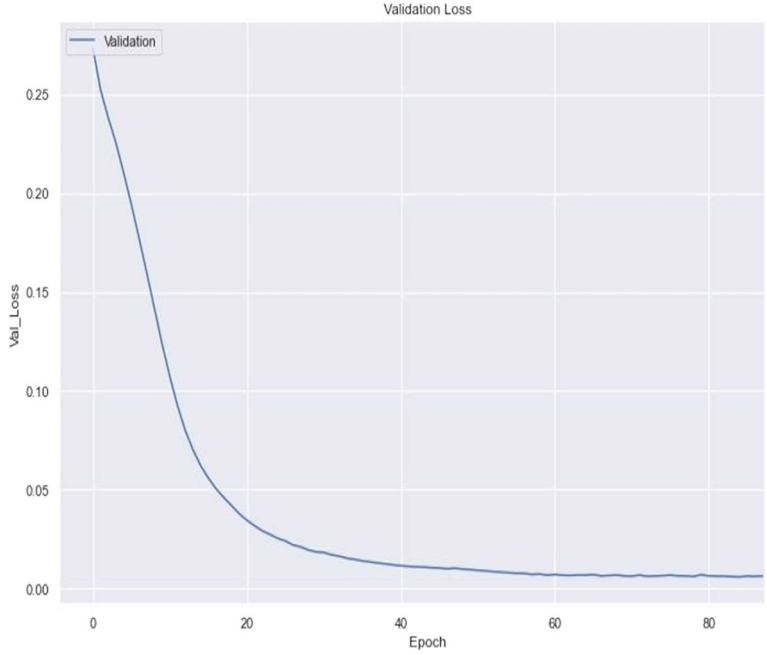


Fig. 11 Validation Loss for SNP dataset

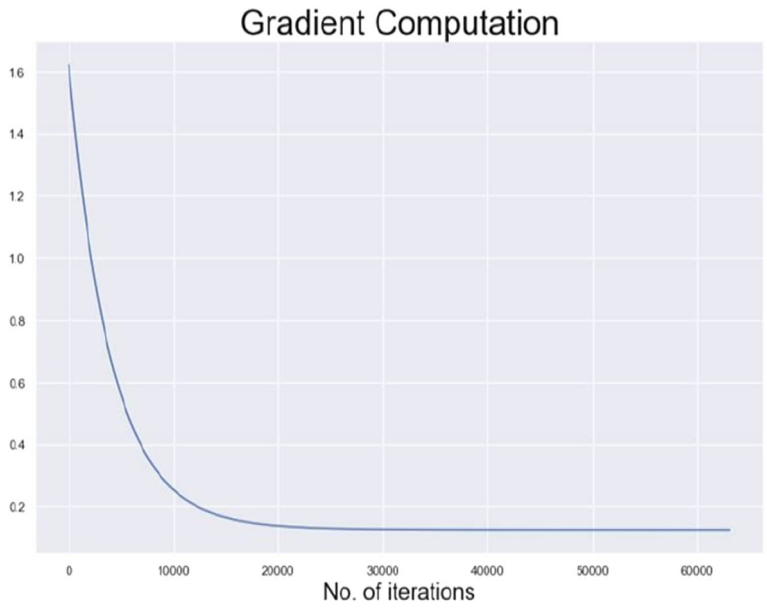


Fig. 12 Gradient Computation

Moderate Demented we are calculating the values represent the micro average ,macro average ,weighted average and sample average which is obtained from precision ,recall and f1 score metrics for all the four deep learning framework.

7.1 Implementation of the datasets using densenet (added point 3)

Table 6 represents the important parameters DENSENET deep learning framework on Alzheimer's data set.

7.2 Implementation of datasets using resnet 50

Table 7 represents the important parameters DENSENET deep learning framework on Alzheimer's data set.

7.3 Implementation using efficient net

Table 8 represents the important parameters EFFICIENT NET deep learning framework on Alzheimer's data set.

Table 4 Model of Error values

Mean Absolute Error	0.025433765
Mean Squared Error	0.01370492
Root Mean Squared Error	0.117068014

Table 5 Comparison of the classification performance

Approach	Dataset	Training Loss	Validation loss	Accuracy
Islam et al. [2]	OASIS	0.038	0.3907	93.18
Ruoxuan et al. [6]	ADNI	0.046	0.31	89.69
Proposed	SNP	0.0224	0.03	99.2

Table 6 Important parameters

	Precision	Recall	F1-score	Support
Non-Demented	0.00	0.00	0.00	57
Very Mild Demented	0.00	0.00	0.00	45
Mild Demented	0.22	1.00	0.36	32
Moderate Demented	0.00	0.00	0.00	10
Micro avg	0.22	0.22	0.22	144
Macro avg	0.06	0.25	0.09	144
Weighted avg	0.05	0.22	0.08	144
Samples avg	0.22	0.22	0.22	144

Table 7 Important parameters

	Precision	Recall	F1-score	Support
Non-Demented	0.00	0.00	0.00	32
Very Mild Demented	0.00	0.00	0.00	10
Mild Demented	0.22	1.00	0.36	57
Moderate Demented	0.00	0.00	0.00	45
Micro avg	0.22	0.22	0.22	144
Macro avg	0.06	0.25	0.09	144
Weighted avg	0.05	0.22	0.08	144
Samples avg	0.22	0.22	0.22	144

Table 8 Important parameters

	Precision	Recall	F1-score	Support
Non-Demented	0.00	1.00	0.00	57
Very Mild Demented	0.00	0.00	0.00	45
Mild Demented	0.22	1.00	0.36	32
Moderate Demented	0.00	0.00	0.00	10
Micro avg	0.22	0.22	0.22	144
Macro avg	0.06	0.25	0.09	144
Weighted avg	0.05	0.22	0.08	144
Samples avg	0.22	0.22	0.22	144

Table 9 Important parameters

	Precision	Recall	F1-score	Support
Non-Demented	0.00	0.00	0.00	57
Very Mild Demented	0.00	0.00	0.00	45
Mild Demented	0.22	1.00	0.36	32
Moderate Demented	0.00	0.00	0.00	10
Micro avg	0.22	0.22	0.22	144
Macro avg	0.06	0.25	0.09	144
Weighted avg	0.05	0.22	0.08	144
Samples avg	0.22	0.22	0.22	144

7.4 Implementation using VGG net

Table 9 represents the important parameters DENSENET deep learning framework on Alzheimer's data set.

8 Conclusion

A subclass of feed-forward neural networks is CNNs. For picture recognition and classification, it is the most useful deep learning approach. The approaches mentioned in this study effort for diagnosing Alzheimer's illness using deep learning are incredibly successful. 95.448 per cent of the training dataset is accurate. On the SNP dataset, the model had 99.2% accuracy. The output includes a Validation Loss graph, a Train Loss graph, and a Gradient Computation graph. The implementation of the proposed methodology is done over Python. Additionally, it displays the datasets for the Moderately Demented, Mildly Demented, and Non-Demented Classes. New Alzheimer's disease therapeutic targets are being established, new agents are being developed, innovative clinical trial designs are being introduced, a broader range of populations are being included in clinical trials, and new biomarkers that provide insight into the impact of emerging therapies are being developed. Drug development success rates are expected to improve.

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Data availability Not applicable

Code availability Not applicable

Declarations

Conflict of interest The authors declared that they have no conflicts of interest to this work. We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

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