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Deep Learning Techniques for Early Detection of Alzheimer's Disease: A Review

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ABSTRACT- Alzheimer's disease (AD) is the most prevalent kind of dementia illness that can significantly impair a person's capability to carry out everyday tasks. According to findings, AD may be the third provoking reason of mortality among older adults, behind cancer and heart disease. Individuals at risk of acquiring AD must be identified before treatment strategies may be tested. The study's goal is to give a thorough examination of tissue structures using segmented MRI, which will lead to a more accurately labeling of certain brain illnesses. Several complicated segmentation approaches for identify AD have been developed. DL algorithms for brain structure segmentation and AD categorization have gotten a lot of attention since they can deliver accurate findings over a huge amount of data. As a result, DL approaches are increasingly favored over cutting-edge Machine Learning (ML) techniques. This study provides you with an overview of current trend deep learning-based segmentation algorithms for analyzing brain Magnetic Resonance Imaging for the treatment of AD. Finally, a conversation on the approaches' benefits and drawbacks, as well as future directives, was held, which may help researchers better comprehend present algorithms and methods in this field, and eventually design new and more successful algorithms.

General Terms: Deep Learning, Alzheimer's disease.

Keywords: Alzheimer's disease (AD), ensemble computing, graph CNN, pulmonary, Adaboost and Neurocognitive.

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1. INTRODUCTION

With the growing need for better healthcare services, substantial research has been conducted over the last decade to develop novel computer simulations for cognitive neuroscience to identify the disease and establish effective treatment methods [5]. This extraordinary achievement has led to an improved considerate of the human brain and its interconnections, thanks to a multidisciplinary approach. Much success has been made in the categorization of neurodegenerative diseases using ML, as shown in *figure 1*, which also reflects existing research patterns in ND classification utilizing deep learning (DL) approaches. The annual trending statistics were found through googling with three-word search keywords.

The keywords– one of the illnesss "AD", "Schizo", "PD" "DL", and "MRI" for years ranging from 2016 to 2021 shown in *figure 1*. PD AD, and other neurodegenerative illnesses are distinguished by the slowing down of normal brain functioning. Several DL approaches for ND identification and categorization of illnesses, particularly their phase, has been developed using a range of neuro imaging modal such that Magnetic Resonances Imaging, CT, PET, and others. Because the number of techniques for analyzing these data is growing, it is critical to analyze the current ones to pick an acceptable methodology for a certain dataset. Several review articles have been written in various directions to produce the concepts of ML and big data in the study of mental health [6][32]. The authors of [22] looked into using DL to understand improved and detect Parkinson's illness. [27] undertook a comprehensive study of DL's application to the interpretation of diverse medical images, including neuro, pulmonary, and pathology.

Most researchers' interest in this topic has recently shifted to caring about it to enhance the superiority of a patient's life and develop medications by studying the pathological procedure associated with various phases of AD. Because AD is a progressive condition, it is divided into four stages: late mild cognitive impairment (LMCI), mild cognitive impairment (MCI), cognitive normal (CN), AD. There are a variety of neuroimaging methods that aid investigators in categorization, the most prevalent of which is MRI.

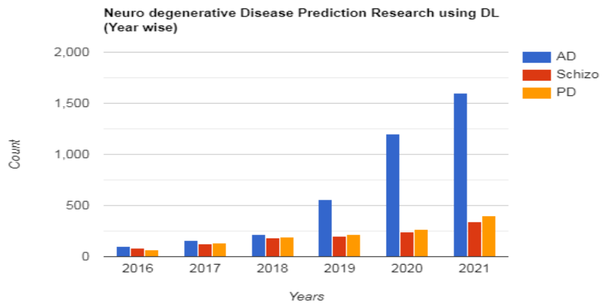

Figure 1: Research count of Alzheimer's disease (AD),

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Schizophrenia (Schizo), and Parkinson's disease (PD) using DL ML is the most frequent and effective technology for diagnosing and classifying diseases with massive amounts of data. The overall goal of this study is to provide an overview of Deep Learning approaches for detecting ND from Magnetic Resonance Imaging as well as its variations. However, due to space constraints, only a cursory examination was conducted and presented in this work. The overall protocol of the proposed study is given in *figure 2*.

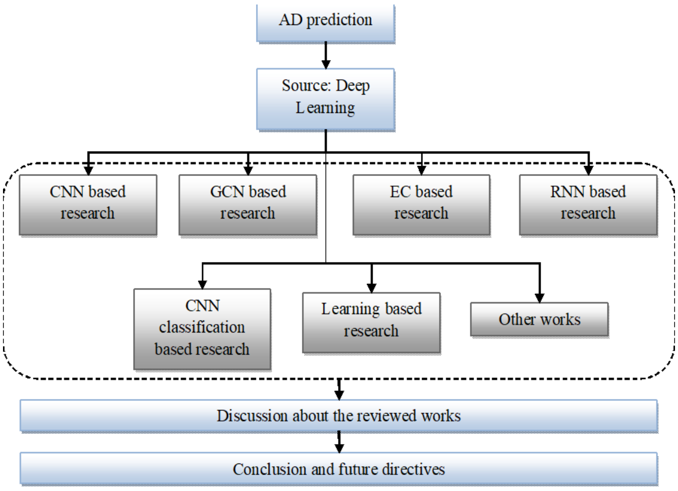

Figure 2: Protocol of the survey proposed

2. REVIEW STUDY ABOUT AD DIAGNOSIS

2.1 Convolution Neural Network Based Review

Developed a novel paradigm for classifying AD and normal cognitive impairment using CNN (NC). The suggested study used CNN feature maps [33] to create a time-to-event prognosis framework with other clinical features relevant to AD dementia, and the model was able to predict patients' progression to AD [7]. The MRI scans obtained from ADNI1 and AIBL2 were used in such an investigation. The experimental dataset was created by slicing the 3D volume of the hippocampal taken from 3D Magnetic Resonance Imaging using a local label learning method. The Convolution Neural Network model used both absent and present extract hippocampus pictures as inputs for label categorization in the suggested strategy. According to Venugopalan et al. [1], each modality can be trained individually. They extracted features from MRI images with 3D-CNN and clinical and genetic information with a stacked denoising auto-encoder. They transmitted the retrieved information from both classifications to the classification layer concatenated. The LASSO regularised Cox regression model is built by combining the training CNN extracted features with the relevant clinical variables [31]. The suggested technique combined CNN with a regression model, with the prediction structure being trained using CNN characteristic maps. However, because two concepts were qualified independently rather than together, it was impossible to merge the regressor and classification as a comprehensive model.

Based on brain MRI, suggested an upgraded inception network to forecast the early stages of Alzheimer's disease [8]. To highlight AD's vulnerable brain areas, image manipulation comprised histogram equalization and multi-threshold classification [13]. The output of the improved change processes was compounded with the output of the basic change processes, which consisted of binary convolution operations (3x3 kernel) with sigmoid function. This extra branch broadened the picture region of interest. It developed the matching concentration heat map, which shows the attention section of MRIs, such as the Hippocampus Region, with all values within the region [0,1]. However, this improved model lacks a mathematical justification for how it emphasizes certain MRI areas.

S. Basara et al. developed a DL model depend on a single cross-sectional brain structural Magnetic Resonance Imaging scan to predict the individualized diagnosis of AD and MCI [9]. This study used data mining algorithms (such as picture rotational movement) to solve the overfitting problem and came up with a good outcome.

Based on MRI scans, that used the Siamese Convolutional Neural Network (SCNN) to categorize AD and NC patients [10]. The suggested SCNN employed three ResNet-34 branches to create three vectors, which served as the extracted feature maps for AD earlier detection. To feed Siamese Convolutional Neural Network on the anchoring and positive branches for 2 network, our approach randomly chose MRI pictures from either the Alzheimer's disease or Normal Controls datasets. One positive pairwise distance was considered using these two parameters. To construct the negative vector, the pictures of the negative branches contain labels against the positive and anchor limbs. The negative pairwise separation, on the other hand, was determined using both the negative and negative vectors. The negative branches, for example, select NC subjects' photographs whereas both the positive and anchor limbs select AD subjects' pictures. In the gradient descent, both positive and negative bilateral relationships were employed, as shown in equations 1.

$$(anch,\ pos,\ neg) = \max\ (\|(anch) - f(pos)\|\ 2 - \|f(anch) - f(neg)\|\ 2 + \alpha) \quad (1)$$

The value α is a margin value. The goal of model training is to make the most of the disparity between pair wise detachment, which implies that as the difference among the anchoring and optimistic pictures grows, so does the difference between both the anchor and negative images. The suggested study aided in the classification of AD and NC subjects using unsupervised reinforcement learning. The CNN's drawback was that it was a classification method, and it could only predict AD versus NC vs MRI.

To predict Alzheimer's disease, devised a representation that included classification and a regression model [11]. Patches of numerous anatomical landmarks made up one portion of the training data, while hand-crafted characteristics like four clinical ratings and two demographic parameters made up the other. The proposed approach began with a two-channel CNN

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that has been trained using landmark patching. Both CNN local features and hand-crafted characteristics were combined in the penultimate layer to create a multiclassifier and ridge regression to forecast scientific score. CNN was used in the research design for both regression and classification.

Deep Convolution Auto encoders (DCA) was proposed to assess the AD state. Grey Matter (GM) and White Matter (WM) areas were segmented from the MRI. DCA was made up of two parts: encoding and decoding. The encoder uses a down-sampling CNN to condense MRI slices into low-dimensional representations, while the decoder uses an up-sampling CNN to reconstitute them. The goal of the training procedure is to reduce the ED between both the unique and reconstruction Magnetic Resonance Imaging, therefore humanizing the effectiveness of compression pictures. SVM and Neural networks were used to categorize the novel representations of Alzheimer's Disease and Normal Control individuals (NN). The model's main flaw was that it attempted to extract patterns in data of distinct MRI classifications in the picture presentation while minimizing loss among input and output images.

To identify AD and Healthy Cognitive (HC), X. Hong et al. developed a novel CNN architecture [18]. The suggested work merged 2D and 3D Convolution Neural Network into2 Convolution Neural Network models, with the characteristic maps exchanged during the execution of the algorithm. The last layer middle output characteristic map of both systems to forecast outcomes. In the CNN model, the suggested technique used both 2D and 3D MRI, but it required a balancing collection and enough MRI pictures.

To categorize AD and Normal Cognitive (NC), A. M. Taqi et al. used a backpropagation algorithm and multiple optimizing compilers [20]. L. Yue et al. suggested a technique for predicting Alzheimer's disease using a custom CNN [21]. U. Senanayake et al. suggested a similar CNN design using dense block and latent block nets to forecast the beginning stages of Alzheimer's disease [25]. The Deep InfoMax (DIM) technique was used by A. Fedorov et al. to construct deep representations of MRIs [12]. DIM is unsupervised representation learning that maximizes the mutual information between a deep neural network encoder's input and output [24]. These studies have shown that data augmentation can successfully reduce overfitting. The best results were attained with the Adam optimizer and RMSProp optimizer. The suggested approaches, on the other hand, were only concerned with identifying Alzheimer Disease and Normal Controls, not with examining model presentation in near the beginning predictions such as Mild Cognitive Impairment.

2.2 Graph Convolution Network (GCN) Based Review

Based on rs-fMRI, proposed a strategy based on Graph Convolution Network to predict MCI [14]. ANDI provided the rs-fMRI dataset for this investigation, which included Late Mild Cognitive Impairment (LMCI), Early Mild Cognitive Impairment (EMCI), and Normal Control subjects. GRETNA3 and DARTEL4 handled the image preparation, which included converting DICOM to NIFTI, temporal splitting, and correction. The proposed technique began using rs-Brain MRI's Functional Connectivity (BFC5) to extract the functional and structural coefficient matrix. To create the subject vectors, every vector was coupled with the subjects' genders, scan device identifiers, and labeling. Each vector was treated as a network, and all interconnections were made depending on how similar these vertices were. Finally, vertices and node edge made up the entire graphs and charts.

2.3 Ensemble Computing Based Review

It used ensemble methods to forecast the premature stages of Alzheimer's disease [26]. The learning database was collected by evenly partitioning 3D-Magnetic Resonance Imaging images into 27 areas and extracting 3D image territory from each area. The height of each patched random vector was reduced using Principal Component Analysis (PCA). The Kmeans classification technique was then used to group the collected portions of each area. To achieve classification, one Dense-Net Convolution Neural Network was attached to each cluster. To accomplish supervised classification, all of the pre-trained Dense-Net CNNs were coupled to a dense coating using SoftMax. The outputs of the pre-trained algorithms were ensembled with the target label using a completely thick network in this study. However, because it was removed from the framework, it is unable to respond to changes in the dataset. In addition, each information cluster required a DenseNet training procedure, which resulted in substantial compute expenses.

For training and testing purposes, the suggested approach employed MRI scans in 3 dimensions. The model contained three channels, each of which was made up of designs from AlexNet, VGG16, and GoogleNet. The three aircraft' MRI scans were then relayed to three separate CNN stations. Equation 2 represents the suggested gradient descent.

$$f(w) = -\log \sum_{k=1}^{M} w_k P_k(C_i \mid x_i^P) - \gamma \sum_{k=1}^{M} w_k \sqrt{\frac{1}{M}\left(\sum_{k \neq n} \left(P_k(C_i \mid x_i^P) - P_n(C_i \mid x_i^P)\right)^2\right)} \quad (2)$$

where w_k are the weights on each subdivision outcomes, and k is the no. of output branches. x_i^p is the picture information at P planes and $P_k(C_i \mid x_i^P)$ is predict possibility of label C_i given an image input x_i^p. Two terms are included in the suggested loss function. The first term calculates the loss of all branch outputs, whereas the second term averages all predicted ranges in the output. The contribution of 2 terms in the gradient descent is controlled by this factor. When this parameter is γ 0, the representation simply analyzes the ratings of each division in the ultimate ensembles. If, on the other hand, increases, the weights are adjusted by taking into account the distance between all branch forecasts. The suggested logistic regression is a system that defines both model training and modeling assembly. Pre-trained models' outputs have also been tailored to target labels with varying effects thanks to upgrades of integrating weights. Nevertheless, the logistic regression does not use the objective brand to generate the defeat, and the classifier is designed unsupervised, thus picture labels are not taken into account throughout the training process, which may have a detrimental impact on simulation results.

2.4 Recurrent Neural Network (RNN) Based Review

The imaging dataset included sMCI6 and pMCI7, as well as longitudinally monitored MRI. To produce deep MRI image descriptions, the suggested technique used a LSTM autoencoder [30]. Information for the multivariate regression was constructed using the representational in combination with custom factors such as hippocampus volume measurements and demographic. Eventually, a Cog multivariate representation was used to forecast the diagnostic achieve for Alzheimer's disease forecast. To categorize the data format, the suggested technique used the K-means clustering t-distribution Statistical Neighbourhood Embedded algorithms (t-SNE). The planned research depended largely on time-series connected to MRI measurement, however, collecting qualitative data with full longitudinally MRI for each patient is difficult. As a result, a lack of information or inadequate data might severely restrict the model's performance.

Multimodal added dimension variation to the collection, allowing MRNN to generate a projection based on all topic information. However, the MRNN classification model consisted of hand-crafted features rather than feature extraction from MRI images, necessitating highly expert data preparation views. Another restriction was the lack of comprehensive-time information. It used Recurrent Neural Network to fill in the gaps in person medical documentation or documentation process to the discontinuous temporal information [16].

The study in this part used RNN to do categorization or construct a data model, with longitudinal studies as the primary training data. However, the study concentrated on merging several important parts of AD patients' knowledge in both words and visuals, rather than on creating detailed data deep features. As a result, poor extracted features of textual information or pictures might significantly hinder the RNN model's comprehensibility.

2.5 CNN Classification Based Review

D. Chitradevi et al. used classification techniques to evaluate brain sub-regions to identify early-stage Alzheimer's disease [3], and the MRI dataset comprised both AD and Normal Cognitive (NC) patients. To improve picture quality, MRIs were subjected to skull stripping and statistical equalization. On MRI, the Grey Matter (GM), Corpus Callosum (CC), Hippocampus Regions (HR) White Matter (WM), were segmented using the multilayer thresholding method. The separated images were then put into CNN to forecast AD. The suggested system used multilayer thresholding to enhance CNN performance and identify AD-related brain areas on MRI. On MRI slices, nevertheless, this automated thresholding approach requires a large distinction here between two consecutive frames. In addition, the segmentation technique used was separated from the CNN model.

The research presented in this part allowed AI algorithms to partition ROI on input pictures for classification or regression. The classification, on the other hand, was based on the image preparation assumptions of regions of the genome, and the segregated data had to be examined by particular specialists to ensure the region's correctness.

2.6 Learning Approaches Based Review

With VGG19 and Brainstorm V4 [29], M. Han et al. used area variation to distinguish AD versus NC. It used transport learning models to examine the identification of AD using MRIs [17]. The suggested learning used the image diversity technique to improve picture selection. Different VGG pre-trained modeling combinations were also evaluated to see whether they could mitigate over-fitting concerns.

The information comprised sliced MRIs from 3 separate planes and developed a novel arrangement integrating Convolution Neural Network and LSTM to identify Alzheimer Disease via domain adaptation [28]. AlexNet, Resnet, VGG-Net, GoogleNet, Squeeze-Net, and Three Decades ago were used to create pre-trained networks. The Squeeze-Net with LSTM achieved the highest accuracy in the planned investigation. Furthermore, the large volume of information may result in the classifier, weakening the pre-trained models.

2.7 Other Approaches

To evaluate hand-crafted characteristics relevant to AD conditions, J. Albright et al. presented an all-pairs approach [19]. These characteristics were used to instruct Neural Network (NN), SVM, Random Forests (RF), Logistic Regression Classifier (LRC), and classifiers to differentiate between Alzheimer's disease and normal cognitive performance (NC). With hand-crafted time-series data taken from Magnetic Resonance Imaging, A. Abrol et al. trained SVM to identify AD versus NC [23]. Random Forest algorithms (RF) were used by X. Hao et al. to optimize characteristic extraction for reproduction development in Alzheimer Disease prediction [4].

Table 1: DL Method Categorization for AD Predictive systems

Ref. No.	Classification (Clas.)/ Regression (Reg.)	Contributions	Data Sets
[7]	Reg.	Convolution neural network output characteristics in a LASSO regularised Cox regression model [2].	Mild Cognitive Impairment & Normal Controls. (MRI) and Clinical Variables
[8]	Clas.	The inception V3 model has been improved.	AD & Normal Controls , MCI & NC, AD & Normal Controls & Mild Cognitive Impairment (MRI)
[9]	Clas.	Data enhancement	AD & Normal Controls (MRI)
[10]	Clas.	3-channel S-CNN	AD & Normal Controls (MRI)
[11]	C&R		pMCI & sMCI & AD & Normal Controls

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		MRI categorization and clinical score reduction using a 2-channel CNN	(MRI) and Clinical Variables
[20]	Clas.	Comparison of different optimizers and feature extraction	AD & Normal Controls (MRI)
[24]	Clas.	Deep CNN for extracting features	AD & Mild Cognitive Impairment & Normal Controls (MRI)
[18]	Clas.	Train the CNN model with 2D and 3D MRI data.	AD & Mild Cognitive Impairment & Normal Controls (MRI)
[12]	Clas.	Deep InfoMax was used to create the MRI deep approximation.	AD & Mild Cognitive Impairment & Normal Controls (MRI)
[14]	Clas.	Graph Cheb-Chevy Neural Network	AD & Normal Controls (MRI)
[15]	Clas.	Image intensity [16] and MRI-trained ensemble multi CNNs on three planes	AD & Normal Controls & Mild Cognitive Impairment
[31]	Clas.	Loss function for deep ensembles generalization	AD & Normal Controls & Mild Cognitive Impairment (MRI)
[17]	Clas.	VGG pre-trained model with image entropy	AD & Normal Controls & Mild Cognitive Impairment (MRI)
[29]	Clas.	VGG16 and Inception V4 (pre-trained)	AD & Normal Controls
[19], [20], [4]	Clas. &Reg.	Hand-crafted features plus machine learning	Public MRIs

3. DATASETS AVAILABLE AND SOFTWARE TOOLS

Although detecting Alzheimer's disease is a difficult undertaking, researchers do not need to work alone. To help, many internet databases and software applications are accessible. FreeSurfer, FSL, MIPAV, and SPM are brain image recognition software that provides strong tools for various automation pre-processing procedures. Deep architectures are implemented using application such that MATLAB, Keras, Tensorflow, Theano, Caffe, and Torch. *Figure 3* depicts the prevalence of each application in our review of the literature. Online databases like ADNI, AIBL, OASIS, and MIRIAD are also quite useful. These databases make indicators including hybrid detection, genomic and blood samples, and physical and cognition evaluations available to the public. ADNI stands out among them all since it is multicenter, persistent research. It is the most commonly used dataset in our evaluation, appearing in nearly 90% of research either alone or in conjunction with each other. ADNI was established in 2003 as a $60 million, 5yrs unrestricted private cooperation involving NIA, NIBIB, commercial firms, and non-profit association. It was a North American-based learning that planned to enroll 800 participants) and monitor them for two to three years. The ADNI method is used to collect this information. Over 50 locations in the US and Canada enrolled ADNI participants aged 55 to 90. The main purpose of ADNI is to see if sequential Magnetic Resonance Imaging, PET, genetics, isolated and identified, clinically, and neurocognitive tests can also be used to pathway MCI and early Alzheimer's Disease development.

OASIS is a project that includes two large datasets for publicly releasing brain MRI information. The cross-sectional database contains Magnetic Resonance Imaging, data from 417 patients varying ages from 18 to 96. The prospective dataset consists of Magnetic Resonance Imaging information from 150 people between the ages of 60 to 96. AIBL, supported by CSIRO is another dataset that contains biospecimen, experimental and PET, cognitive tests, Magnetic Resonance Imaging, lifestyle evaluations. The database is a collection of MRI scan taken from individuals at 2-week to 2-year periods; the original study goal is to see if MRI may be used in clinical studies of AD therapies. Lastly, some researchers choose to use their local data collected. *Figure 3* contains further information about software packages.

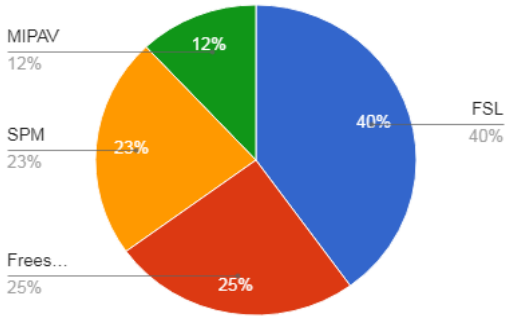

Figure 3(a): DL Software

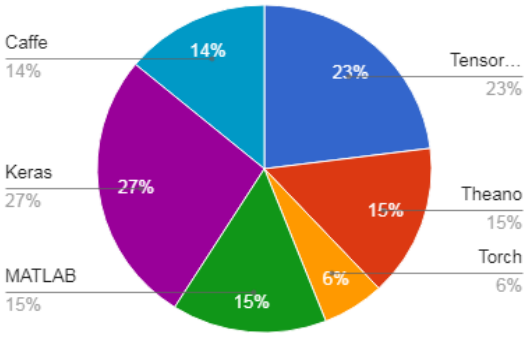

Figure 3(b): Software utilized as per the study

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4. DISCUSSION AND SURVEYED WORKS

It was decided after reviewing the most recent research on Alzheimer's disease early identification. The accompanying points must be considered to achieve optimal improvements and increase the accuracy of diagnosis utilizing a computerized system:

- Acquiring brain-balanced and adequate information on Alzheimer's illness is among the obstacles.
- Deep learning categorization (e.g., U-Nets) can be used to designate only the objects of interest in the procedure.
- It is possible to diagnose AD by combining different theoretical methods: dense analysis and DL. A manifold-based learning approach is also a good approach.
- Approaches such as data preprocessing and scaling can help to increase aggregate state-of-the-art productivity.

5. CONCLUSION

The most frequent kind of later dementia is Alzheimer's disease, which is a cumulative neurodegenerative illness. In the brain, AD induces nerve cell mortality and nerve injury, resulting in a decline in brain size over time and deterioration of most activities. In this research, we discussed the significant differences between standard ML and DL, as well as the stages of AD diagnosis. We really ought to pre-process pictures in the detection of Diseases to improve student learning, thus we demonstrate various data preprocessing approaches. We also discussed other DL approaches that are commonly used in classification, such as Convolutional Neural Network, Recurrent neural networks, Deep Neural networks, AE, and DBN. Despite the importance of utilizing DL to classify diseases, there are obstacles in dealing with the information. As a result, we offered a review of existing literature for each difficulty and demonstrated their solutions. The current latest survey originality may be characterized by introducing several preprocessing approaches that were evaluated.

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