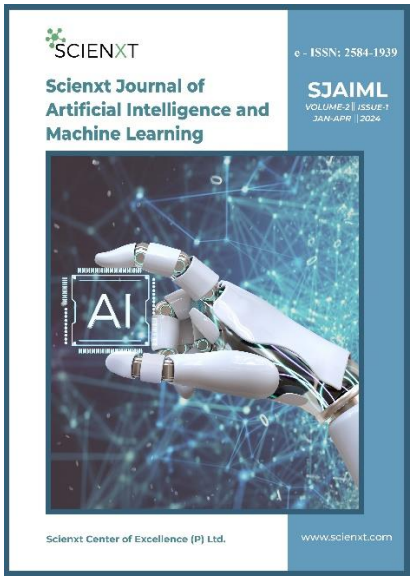

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Utilizing deep autoencoders for extracting key features in alzheimer's disease diagnosis

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Abstract:

This paper introduces a novel approach for extracting features of Alzheimer's disease (AD) from MRI images using a Deep Autoencoder (DAE). Utilizing a custom-made five-layer encoder architecture, feature extraction is made easier. The efficacy of the DAE is meticulously assessed using nine diverse Machine Learning Classifiers. Cross-validation is performed to substantiate the superiority of the DAE's feature extraction by comparing the classification of AD stages with Clinical data. The dataset encompasses distinct stages of AD, enabling a comprehensive analysis. Our results showcase the proposed method's superiority, surpassing clinical data and outperforming related methodologies from other researchers.

Keywords:

Deep Autoencoder (DAE), Magnetic Resonance Imaging (MRI), Alzheimer's disease (AD), Machine Learning, Deep Learning.

1. Introduction:

Alzheimer's disease (AD) is a disorder that gradually damages the brain, affecting the cognition, memory, and behaviour patterns of the human. Classified as a neurodegenerative disease, it impacts up to 5% of people globally [1]. It progresses through stages: Early Mild Cognitive Impairment (EMCI), Mild Cognitive Impairment (MCI), Late Mild Cognitive Impairment (LMCI), and Alzheimer's disease (AD) [1]. AD's onset might occur up to two decades before symptoms manifest [2]. This underscores the importance of early diagnosis for a disease which does not have a cure.

In diagnostics, modern techniques leverage computer- aided approaches to assess AD [2]. Various machine-learning techniques are used to categorize and analyze AD. However, the challenge remains in the limited medical image datasets, which often need proper labelled data. The need to have improved data quality hinders the development of machine- driven diagnostics tools.

Addressing these issues, recent advances in deep learning have shown promising results in areas like feature extraction, segmentation, and classification of medical images. Deep learning techniques are good at dealing with missing data, data scarcity, and poor labelling in medical image data. Among these, unsupervised learning techniques, especially the Autoencoder, stand out. Autoencoders, consisting of encoders and decoders, process input images, extract the features and encode them into a latent space. The decoder then reconstructs images from this encoded information. Various Autoencoder models, which use different techniques to deal with extraction and encoding, have shown remarkable effectiveness in dealing with medical image data like AD data.

This paper proposes a robust feature extraction technique called Deep Autoencoder (DAE). The extracted features isolated by the DAE are then classified into various stages of AD using nine machine learning algorithms, with Radial Basis Function driven Support Vector Machine (RBF SVM)[14] achieving the highest accuracy. Using the same state-of-the-art ML classifiers, a comparison was made between the DAE models feature extraction efficiency and clinical evidence features from the same images. The results show the effectiveness of Deep Autoencoder as an efficient feature extractor.

2. Literature review:

Many works have used deep learning techniques for feature extraction and classification from

AD data. Convolutional neural networks (CNN), Deep Neural Networks (DNN), and Restricted Boltzmann machines (RBM) are the most commonly used DL methods in AD research [11].

F.J. Martinez-Murcia et al. used Deep Convolutional Autoencoder for the AD study. This method best defines the complicated relationship between cognitive symptoms, underlying neurodegenerative processes, and clinical attributes using MRI images using the ADNI dataset. Their work obtained a classification accuracy of eighty percent [1]. Ekin Yagis et al. adopted a three-dimensional VGG (very Deep convolutional Network), a variant of convolutional neural network for AD studies [2] [16]. They used structural MRI to differentiate between AD and Normal patients with the help of OASIS and ADNI datasets. The model obtained classification accuracy of 73.4 percent and 69.9 percent respectively [2].

Walter H. L. Pinaya et al. proposed a technique called Normative Models using DeepAutoencoder (DAE). The study, which used MRI data from the UK Biobank dataset, examined AD and MCI classes and gave an average classification accuracy of 91.2 percent [3]. Pushkar Bhatkoti et al. introduced a method called Modified Sparse Autoencoder. The method, which used a combination of MRI and PET scans, tried to create connections between localized degenerative brain regions and obtained 79.22 % accuracy in classifying individuals with AD and CN [4].

Ricardo Mendoza-Léona et al. suggested Supervised Switching Autoencoders (SSA). Using structural MRI (sMRI) data from the ADNI dataset, the study classified patients with AD and normal participants and demonstrated an average accuracy of 90 percent [5]. Raffaele Ferri et al. proposed a method called Stacked Autoencoders (SAE) using resting-state electroencephalography (rsEGG) and MRI scans of both normal and AD patients. The method obtained an accuracy of 86.5 percent by combining the ADNI and OASIS databases [6].

Hamid Akramifard et al. offered an Autoencoder Neural Network (AENN), a technique for classifying distinct cognitive states-MCI vs CN, MCI vs AD, and CN vs AD. Across all of these categories, their approach produced an accuracy of 93.4 percent. Using machine learning methods for cross-validation, the methodology produced an accuracy of 92.2 percent with Support Vector Classifier (SVM) [7]. Simultaneously, Rohollah Hedayati et al. developed a methodology based on a Pertained Autoencoder (PAE) working as a feature extractor with Convolutional Neural Networks (CNN). A comprehensive approach was used to distinguish between the MCI versus AD and MCI versus CN. The method achieved 92.5 percent accuracy [8].

Janani Venugopalan et al. introduced a novel method, termed the Fuse Model, a combination of Stacked Denoising Autoencoders (SDAE). It integrated 3D Convolutional Neural Networks (3DCNN) in parallel to analyze MRI images using Stacked Denoising Autoencoders (SDAE) for genetic and clinical data. They tested the fusion model's performance against a range of ML classifiers through robust cross-validation. Surprisingly, the fusion method performed much better, with an accuracy of 89.5% [9].

Ramon Landin-Romero et al. introduced a free surfer using Linear Fixed Effect Modeling to classify AD and Normal to find an area of cortical and subcortical structures of brain regions [12]. Agneta Nordberg, Juha O.et al. used a method using PET images to understand the growth of proteins that cause Alzheimer's disease [13]. Simeon Spasov et al. proposed deep learning techniques and machine learning classifiers to classify AD and Normal [14]. S. Leandro et al. proposed using MRI images to access AD at an early stage using cerebral atrophy [15].

In the context of the above studies, we propose a method to extract AD features using a deep autoencoder and classify various AD phases using different ML classifiers. Our proposed method differs from the above in three ways. Firstly, we used all the stages of AD, such as EMCI, MCI, LMCI, CN, and AD, in the study. Secondly, features were extracted using Deep AE, and their effectiveness was cross-validated with nine ML classifiers. Lastly, we again compared the effectiveness of features extracted by DAE with clinical data features and were classified using the same ML classifiers.

3. Materials & methods:

The conceptual framework of our proposed work is illustrated in Fig. 1, delineating the critical aspects of our approach. It involved different steps like data collection, pre-processing of data, feature extraction using Deep AE, cross-validation using different ML algorithms, and further validation using clinical data.

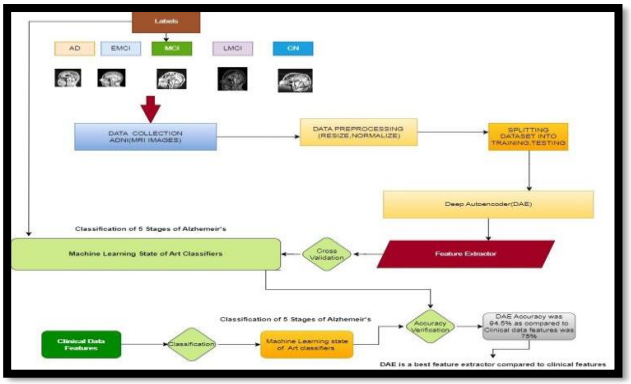

Figure. 1: Proposed work

3.1. Dataset:

The Proposed work uses a dataset from the Alzheimer's disease Neuroimaging Initiative (ADNI) [10]. Notably, different MRI protocols were employed following the manufacturer's recommendation. Medical experts emphasize the accuracy of MRI biomarkers for predicting Alzheimer's disease. MRI images provide intricate details of the brain structure, offering clear visualization of soft tissue and cerebrospinal fluid (CSF), along with the essential white matter and grey matter (WM & GM) [10]. The MRI imaging protocol encompassed specific parameters: T1 weighted, 3D (MPRAGE), sagittal acquisition plane, Field strength of 1.5 tesla, and Flip Angle at 8.0 degrees. The manufacturer was GE, and the model was SIGNA EXCITE. Pixel spacing of 0.9mm in both x and y directions and slice thickness of 1.2mm were used. Importantly, Repetition Time (TR), Echo Time (TE), and Inversion Time (TR) were specified as TE=3.9 ms, TI=1000.0 ms, and TR=8.9 ms, respectively [10].

The study used 500 samples with 100 data points taken from the ADNI dataset, each representing one of the five stages (EMCI, LMCI, MCI, and AD & CN). Table I gives detailed demographic information of the patients whose data were used for the study [10].

Table. I: Demographic details of persons belonging to different stages of AD used in the study

MRI Stages	Age group
CN	60 to 91
EMCI	56 to 89
MCI	55 to 89
LMCI	55 to 89
AD	50 to 93

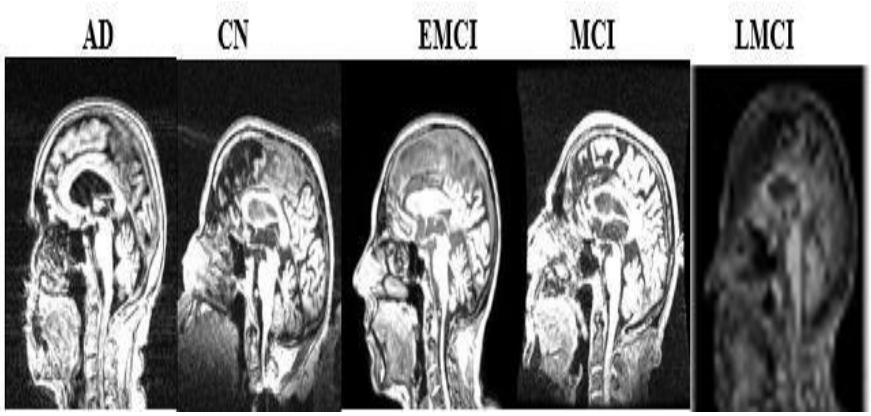

Figure. 2: MRI images illustrate different stages of Alzheimer's disease

Fig. 2 shows the sample MRI images of 5 stages of sagittal view.

3.2. Pre-processing:

In response to the observed inconsistencies in MRI image sizes originating from different manufacturers, a vital pre- processing step was introduced: standardizing the dimensions of input MRI images [10]. This pre-processing procedure ensures that our approach maintains uniform image dimensions across different stages of Alzheimer's disease, thereby guaranteeing consistency in subsequent analyses. For our research, 500 MRI images sourced from ADNI datasets were employed. These images were pre-processed to maintain a standardized size of 192x192 pixels. These pre- processed images serve as the input data for our Deep Autoencoder (DAE) model.

3.3. Feature extraction using DAE:

The pre-processed data undergoes Deep Autoencoder (DAE) training to extract relevant features. This process involves partitioning the pre-processed MRI images into a 70:30 train-test ratio. Including all five stages of Alzheimer's disease, the training data feeds the DAE, with its architecture depicted in Fig. 3.

Specifically, only the encoder component of the DAE is employed for feature extraction. This encoder comprises five layers, with node quantities determined after comprehensive investigation: 18,432 nodes in the first layer, 9216 nodes in the second, 1,280 nodes in the third, 64 nodes in the fourth, and 32 nodes in the final layer. The last year's output forms an encoded vector, collectively generating the latent space. This latent space effectively captures the extracted features from MRI images across all five stages of Alzheimer's disease. Subsequently, the decoder aspect of the DAE transforms these features to facilitate image reconstruction.

3.4. Classification of features using machine-learning classifiers:

The encoded vectors, representing the extracted features in the latent space, are combined with the corresponding labels denoting the stages of Alzheimer's disease, forming the input for various machine learning classifiers. In our proposed methodology, nine distinct classifiers were employed, namely: Nearest Neighbor Classifier (NNC), Linear Support Vector Classifier (LSVC), Radial Support Vector Machine (RBFSVC), Decision Tree Classifier (DTC), Neural Network Classifier (NNC), Random Forest Classifier (RFC), AdaBoost Classifier (ABC), Naive Bayes Classifier (NBC), and Quadratic Discriminant Analysis (QDA).

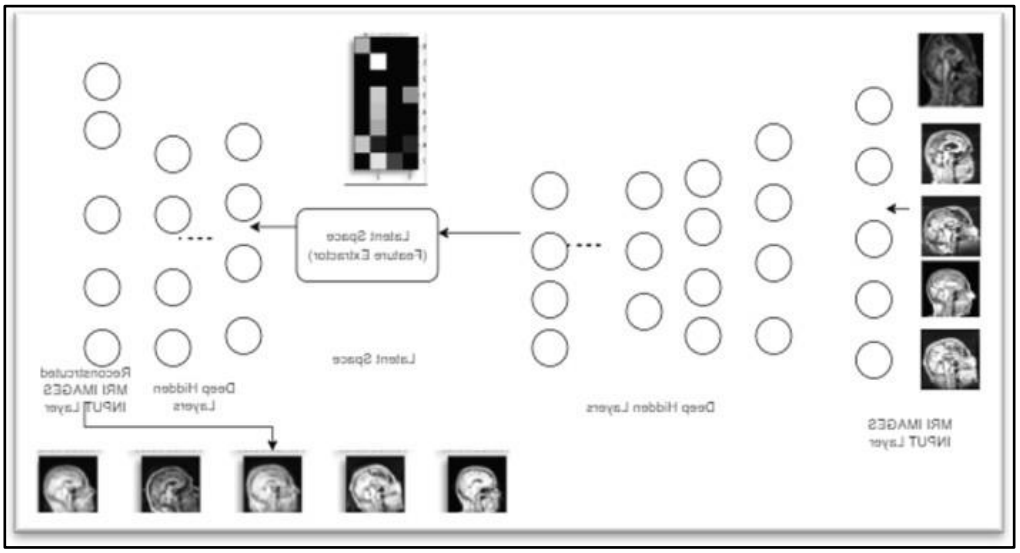

Figure. 3: Deep autoencoder (DAE)

The performance of each classifier was meticulously recorded, and the classifier demonstrating the highest accuracy was selected as the optimal model for classifying the features extracted by the DAE. This systematic approach ensures that the most accurate classifier is chosen for classifying the intricate features derived from the DAE's output.

3.5. Cross-validation using clinical data:

To comprehensively validate the efficacy of the Deep Autoencoder (DAE) in extracting features from distinct stages of Alzheimer's disease, we undertook a parallel approach using the corresponding clinical data for the same images, as outlined in Table II below.

These clinical data were subsequently incorporated into each classifier for classifying the extracted features. A thorough comparison of the performance of each classifier was conducted, and the accuracy of the classifier yielding the most favourable results was chosen for comparison with the accuracy of the features extracted by the DAE. By posing the classifier's performance on clinical data with that on DAE- extracted features, we sought to ensure a robust evaluation of the DAE's capability in feature extraction across various stages of AD.

3.6. Experimental setup:

The methodology was executed using Keras version 3.4.3, harnessing the computational capabilities of an NVIDIA GeForce RTX 2080 Ti GPU with 12GB VRAM. A proper batch size was employed to facilitate efficient processing. For the architecture of the Deep Autoencoder (DAE), each layer was configured with Rectified Linear Units (ReLU) as nonlinear activation functions [6]. The optimization of loss functions was achieved through the utilization of the Adam Optimizer.

Several hyperparameters played a pivotal role: The activation function was the sigmoid function, the learning rate was set at 0.0001, and the loss function was the mean squared error (MSE). The Deep AE network underwent 100 epochs, with diverse iterations observed at intervals of 25, 50, and 100 epochs to assess performance fluctuations throughout the training process.

In addition to the MRI images, which were used to extract features using Deep Autoencoder, the study also used clinical data to compare the performance of the DAE model. The clinical data set was a CSV file containing different features corresponding to age and specific diagnostic findings. The various characteristics and range of values of the used clinical data are described in detail in Table. II.

Table. II: Clinical data features and their description [10]

Clinical Data features	**Description of features**	**Normal Patient**	**EMCI**	**MCI**	**LMCI**	**AD**
Age	The age range is considered from 55 to 93 years, a critical factor in disease analysis.	60 to 91	56 to 89	55 to 89	55 to 89	55 to 93
APOE A1	A gene encoding Apo lipoprotein E, with variants APOE A1 and alleles €2, €3, and €4. APOE A1 increases Alzheimer's risk	3	2, 3 and 4	2 and 3	2,3 and 4	4
APOE A2	A gene encoding Apo lipoprotein E, with variants APOE A2 and alleles €2, €3, and €4. APOE A2 Alzheimer's reduces risk.	4	3 and 4	3 and 4	3 and 4	4
NPI-Q Total Score	The Neuropsychiatric Inventory Questionnaire gauges disease severity and neuropsychiatric symptoms.	0 to 9	0 to 14	0 to 16	0 to 16	0 to 30

MMSE Total Score	Mini-Mental State Exam, a cognitive test to assess memory and cognitive functionality.	0 to 11	22 to 30	16 to 30	16 to 30	0 to 29
GDSCALE Total Score	Gottfries-Brane-Scale measures cognitive function in Alzheimer's patients.	-1 to 0.5	0 to 6	0 to 13	0 to 13	0 and 4
FAQ Total Score	Frequently Asked Questions delves into reasons behind Alzheimer's development.	0 to 11	0 to 13	0 to 22	0 to 22	0 to 30

Abbreviations used in Table. 2

APOE A1 and A2- Apo lipoprotein E

NPI-Q-Neuropsychiatric Inventory Questionnaire

MMSE - Mini-Mental State Exam

GDSCALE-Gottfries-Brane-Scale

FAQ-Frequently Asked Questions

4. Results:

4.1. Epoch iteration: 100 (testing vs training):

Illustrated in Fig. 4, the network's learning progression is depicted as it assimilates features from MRI images across various stages of Alzheimer's disease. The gradual and consistent curve advancement signifies a methodical and steady learning process. This observation underscores the network's capacity to adeptly comprehend and learn the intricate features, as a measured and smooth curve progression indicates more precise and accurate feature

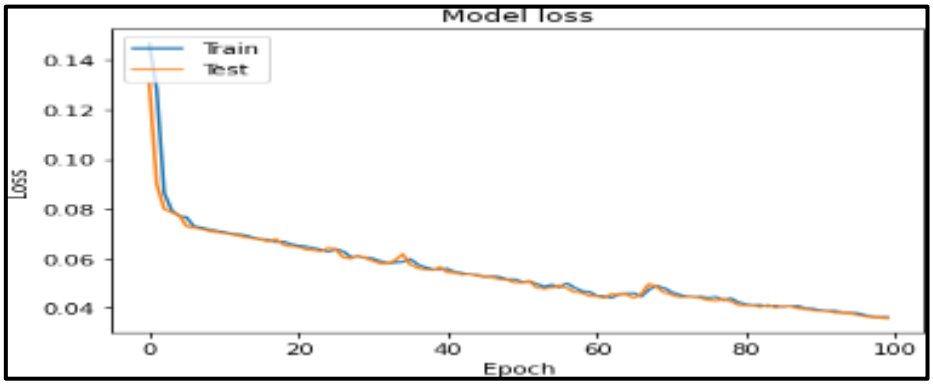

Figure. 4: Epoch 100

acquisition.

Original, Reconstructed, and Encoded images. Presented in Fig. 5 is a depiction of the DAE's impact, showcased through a triptych of image rows. The initial row showcases the unaltered images in a 192x192 pixel format, which serves as input for the DAE. The decoder's output is unveiled in the subsequent row, exhibiting the reconstructed images. The last row shows the encoded vectors originating from the DAE encoder. These encoded vectors show the network's ability to identify the various stages of Alzheimer's disease, capturing the distinctions in the Latent space or Encoded vector.

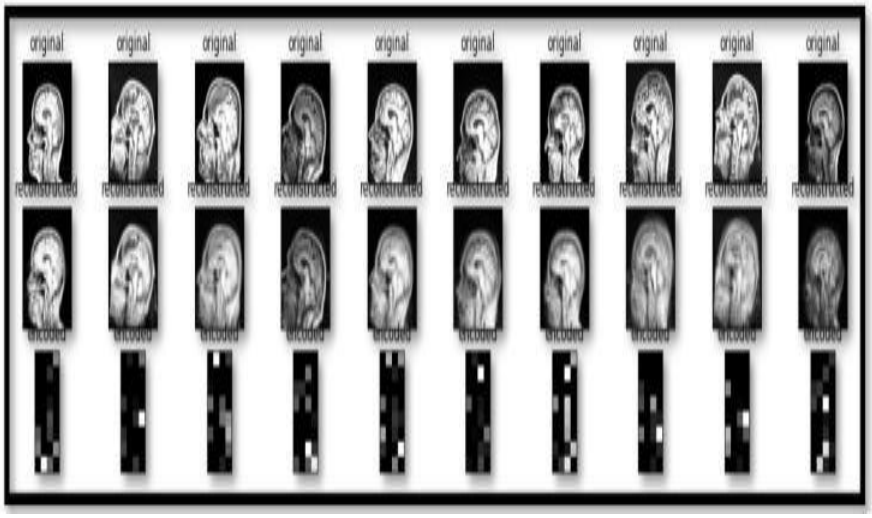

Figure. 5: Original images - reconstructed images - encoded vectors

4.2. Transformation of one image:

Fig. 6 shows the path of a single image through the process to give a thorough understanding of the transformation process that was previously explained. It features three parts- the original image, the corresponding decoded image, and the encoded image. This sequence demonstrates the variance in feature representation, distinguished by varying shades of grey and distinct white blocks. This visualization is particularly insightful as it encapsulates the essence of the transformation process, providing an in-depth perspective on the encoding and decoding pathway of an individual image sample.

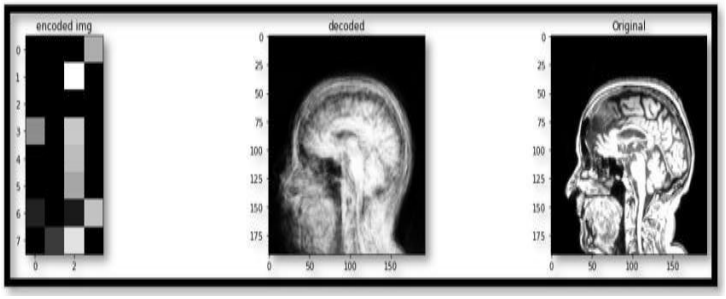

Figure. 6: Image transformation Process

4.3. Epoch vs accuracy:

The accuracy that the Deep Autoencoder (DAE) algorithm achieves over a range of epoch values is graphically represented in Fig. 7. The network obtained an accuracy of 85.12% at epoch 25, which is significant since it indicates the early phases of learning. By the time it reached epoch 50, the accuracy had significantly improved to 89.23 percent, highlighting the network's increasing competence. Significantly, the accuracy reached its peak of 94.5 percent at epoch 100, showing the network's logical and consistent growth. This accuracy enhancement timeline reveals how and why the network progressively evaluated and predicted the complex aspects in MRI images across different stages of Alzheimer's disease.

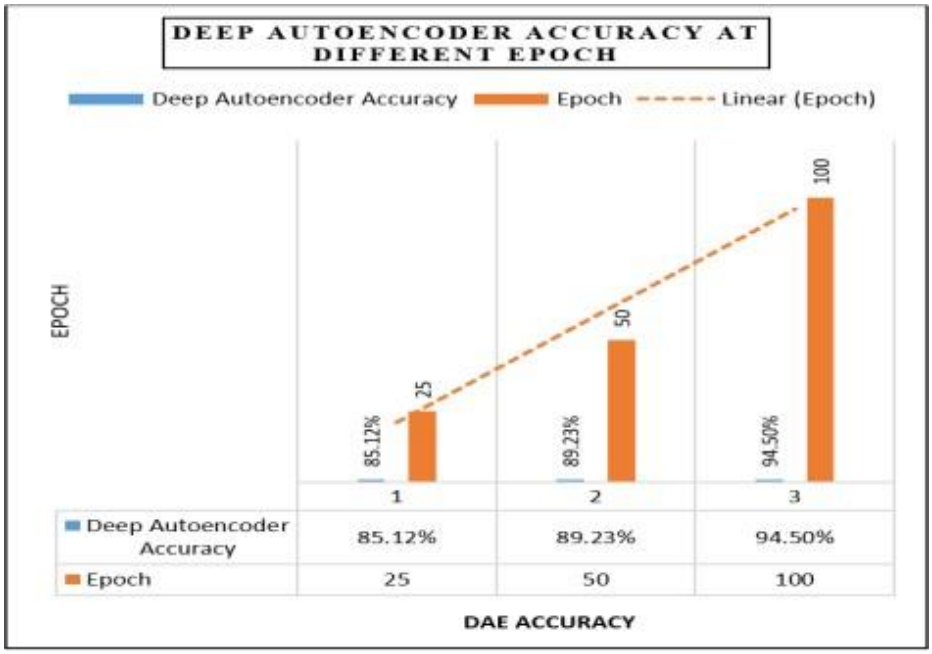

Figure. 7: Accuracy vs Epoch

4.4. Performance of classifiers:

In Fig. 8, the Deep Autoencoder (DAE) feature extractor and clinical data features-two different feature sources-are extensively evaluated to classify different stages of Alzheimer's disease. Nine ML classifiers are used here for comparative study. The Radial Basis Function Support Vector Machine (RBF SVM) was the best classifier in both methods.

The accuracy of the results gained, however, is what sets them apart. The clinical data features produced an accuracy of 75%, but RBF SVM used the Deep Encoder feature extractor provided 94.5% accuracy in detecting the Alzheimer's stages. This striking disparity highlights how the DAE-based feature extraction strategy is better while identifying the various phases of Alzheimer's disease.

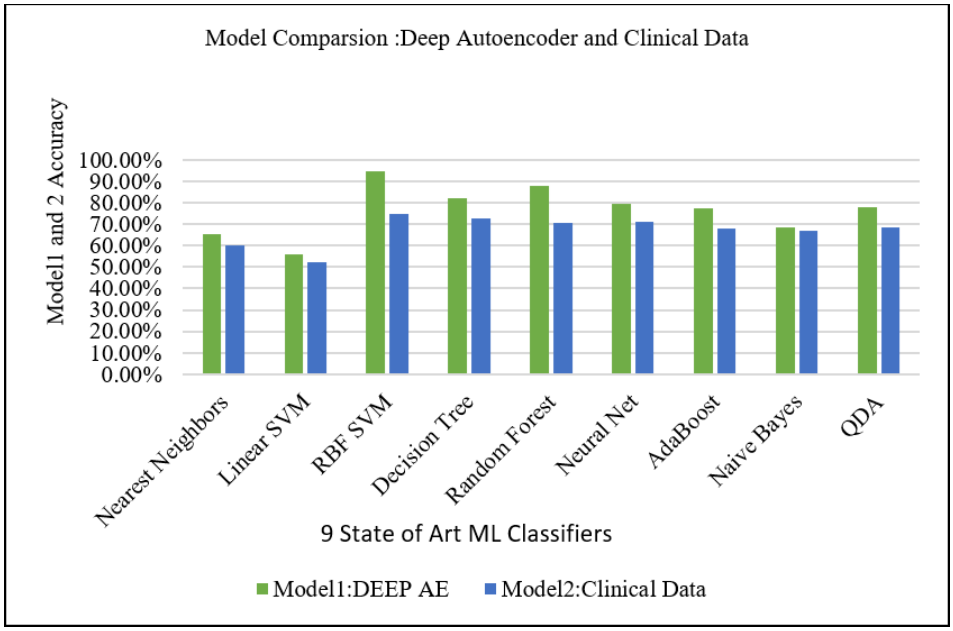

Figure. 8: Model comparison

4.5. Comparative chart of Testing vs. Training Accuracy at Epoch 100:

Fig. 9 shows the comparison of accuracy values achieved in the training and testing stages at epoch 100. Specifically, the testing accuracy was 94.5 %, showing the model's ability to classify Alzheimer's stages correctly. Similarly, the training accuracy achieved a notable 92.10 %. This shows there is a very small overfitting happened and the model results can be generalized.

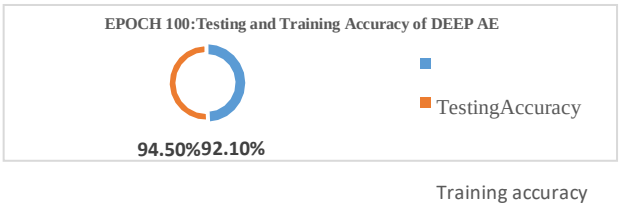

Figure. 9: Training vs Testing Accuracy at Epoch 100

4.6. Comparison with other related works:

Table. III provides a detailed comparison between proposed work and related studies based on six criteria. Firstly, the methods employed are scrutinized and compared based on datasets. The type of medical images utilized is the third parameter, whereas the classification accuracy is the fourth. Moreover, the table evaluates whether clinical features were utilized for comparison or not, and finally, it enumerates the stages of Alzheimer's disease (AD) that were included in

the respective studies. The table shows that our proposed work consistently outperforms other related studies across these diverse criteria.

Table. III: Comparison with other related works

Author's	**Metho ds used**	**Dataset s used**	**Type of Medical images**	**Classifi cati on Accura cy**	**Clinical features used or not**	**Stages of Alzheime r's classified**
F.J. Martinez-Murcia et al	Deep Convol utional autoen coders	ADNI	MRI	80%	NO	AD and CN
Ekin Yagis et al	3D VGG variant convol utional neural networ k	ADNI &OASI S	MRI	73.40%	NO	AD and CN
Walter H. L. Pinaya et al	Deep autoen coders (DAE)	UK Bioban k	MRI	91.20%	NO	AD and MCI
Pushkar Bhatkoti et al.	Modifi ed sparse Autoen coder	ADNI	MRI and PET	79.22 %	NO	AD and CN
Ricardo Mendoza-Léona et al.	Superv ised switchi ng Autoen coders	ADNI and OASIS	MRI and rs EGG	90%	NO	AD and CN
Hamid Akramifar d1 et al	Autoen coder Neural Netwo rk	ADNI	MRI	92.20%	NO	MCI/CN, MCI/AD, CN /AD
Rohollah Hedayati et al	Pretrai ned Autoen coder and CNN	ADNI	MRI	92.50%	NO	MC/CN and MCI/AD
Janani Venugopa lan et al	Stacke d denoisi ng auto- encode rs and 3DCNN	ADNI	MRI	89.50%	YES	AD and CN
Proposed Work	Deep autoen coders (DAE)	ADNI	MRI	94.50%	YES	EMCI, MCI, LMCI, AD and CN

4.7. Superiority of proposed work in terms of classification accuracy:

A prominent highlight within Table III is our method's remarkable accuracy, which gains further prominence in Fig. 10. This visualization succinctly demonstrates the relative

significance of accuracy, emphasizing that our proposed work has achieved an accuracy of 94.5%. This figure reinforces the superiority of Deep Autoencoder over other existing methods to extract features of different stages of AE.

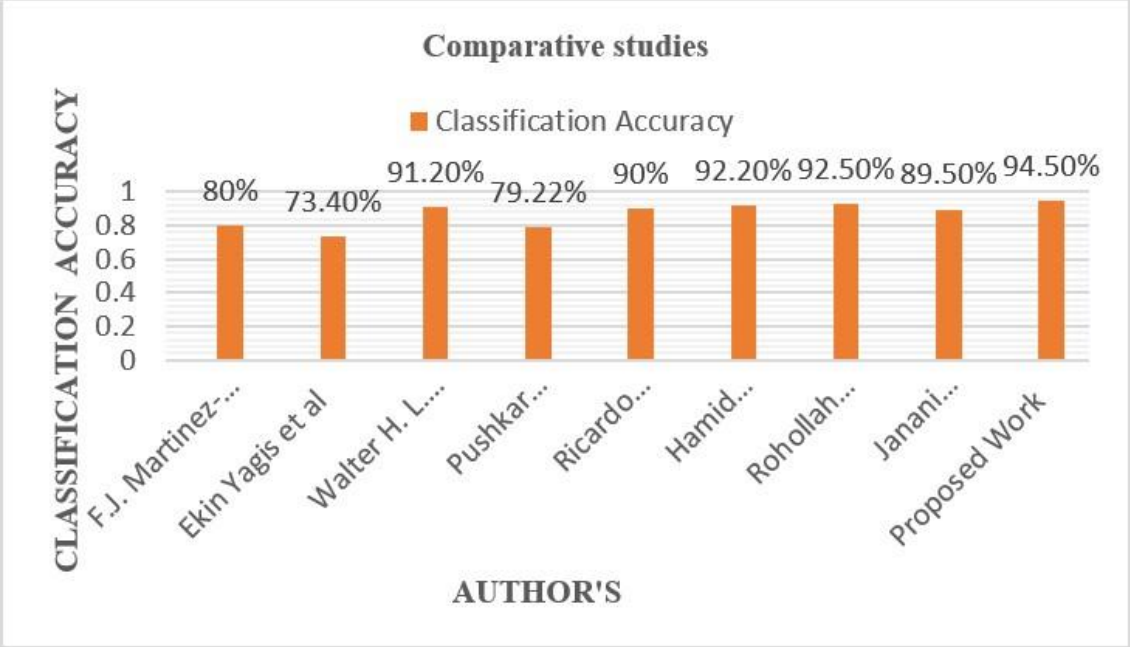

Figure. 10: Comparative Classification Accuracy vs Authors

5. Conclusion:

This paper introduces Deep Autoencoders as a feature extraction technique for AD diagnosis. Using MRI data, DAE extracts features at various stages of Alzheimer's disease. Our investigation establishes DAE as the preeminent feature extractor, attaining a remarkable accuracy of 94 percent, which is far superior to the accuracy delivered by clinical data features. Through a comprehensive comparative analysis between our method and the other related works, as well as with clinical data, the study shows the superiority of DAE as a feature extraction technique for the MRI images of AD. As the natural progression of our research, the proposed methodology serves as a stepping-stone for more advanced studies, mainly focusing on Progression Analysis and Early Detection of Alzheimer's Disease.

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