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Prediction of Alzheimer's disease Using Stacked Ensemble Transfer Neural Network Model

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Abstract: It is studied that Alzheimer's disease (AD) is growing fast and main cause of the death for the elderly people. Early detection of Alzheimer's disease has been proven to enhance patient outcomes. Machine learning techniques that utilize magnetic resonance imaging (MRI) have been used for AD diagnosis, but traditional methods require manual feature extraction by an expert, which can be complex. To address this, our study proposes a new approach using a pre-trained convolutional neural network called Stacked Ensemble Transferred Neural Network (SETNN) model for automated features extraction when using MRI images to detect Alzheimer's disease. The effectiveness of the SETNN model was assessed using a number of criteria, including accuracy, in comparison to traditional Softmax and support vector machine (SVM) techniques. The outcomes shown that, when applied to the MRI images from the ADNI dataset, the proposed SETNN model outperformed existing state-of-the-art models, achieving 99.49% accuracy. The developed model shall improve the prediction efficiency and decision making with early detection of Alzheimer.

Keywords: *Brain imaging; convolutional neural network (CNN); Alzheimer's disease; pre-trained model; Ensemble learning*

1. Introduction

A long-term neurological condition called Alzheimer's disease mainly causes neurodegeneration in middle-aged and older people [1]. It can be a long-term, incurable illness having an elevated risk of failure in treatments for Alzheimer's [2]. The progressive loss of memory and other cognitive functions over time is the pathologic characteristic of Alzheimer's disease [3]. This disease's current clinical diagnosis is a time-wasting endeavour with no hope of success [4]. In 2006, there were more than 26 million Alzheimer's patients worldwide [5]. While [6] estimates that approximately 50 million individuals worldwide suffering from dementia, by 2050, this number is expected to rise to 31 to 152 million, especially in low- and middle-income nations, making dementia a major worry for the future century. According to [7], AD deteriorating mental state of patient to the point where they are unable to carry out daily tasks without the assistance of family members [8]. Nonetheless, Alzheimer's disease can be slowed down in its progression with early detection and treatment [9].

AD primarily impacts brain regions that control memory and language, resulting in loss of memory, ambiguity, and troubles in verbal and written communication [10]. Currently, AD and HC can achieve above 90% accuracy using imaging materials, whereas MCI and HC have relatively poor accuracy. The low early diagnosis accuracy can be attributed to two key factors. In the beginning, brain atrophy is a slow process [11] that is relatively mild and challenging to identify. Second, the natural ageing of the brain in healthy persons and the brain shrinkage of early-stage MCI patients have certain similarities in the data space [12]. CT scans and MRIs provide important insights into the study of the neurological system and the characteristics of the brain, which is necessary to fully evaluate the condition and finally determine the most accurate ways to identify Alzheimer's disease. As a result, they can be used in conjunction with CAD systems [13], assisting clinicians in avoiding misdiagnosis due to inexperience or exhaustion. Furthermore, it could offer previous and much more accurate diagnosis, lowering the costs of caring for Alzheimer's patients [14].

Many efforts have been made to create an accurate and trustworthy substitute for the fully automated identification of Alzheimer's disease. Traditional machine learning (ML) techniques depend on characteristics that are manually generated, which weakens the solution's resilience. Conversely, deep learning-based systems yield far better results by automatically extracting meaningful characteristics [15]. For training, deep learning-based methods need a lot of labelled data, which is hard to come by. In order to categorise various MRI and fMRI image datasets using binary and multi-class methods, Loddo et al. [1] used a deep ensemble technique combining Inception-ResNet-v2 with AlexNet and ResNet-101. To improve the quantity of imagery prior to training the

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model, the study also employed data augmentation. With regard to binary classification, their suggested model achieves 98.51% accuracy, while for multiclass classification, it reaches 98.67%. Mahendran et al. [2] used a deep learning architecture with a feature selection algorithm included. This process involved the use of standard machine learning techniques for feature selection and k-folds cross-validation for model evaluation. Sava [3] utilised several CNN architectural models to categorise different phases of Alzheimer's disease on an ADNI dataset. They tested the accuracy, precision, sensitivity, and specificity of 29 pre-trained models using MRI scans. EfficientNetB0 achieved a high accuracy of 92.98%, whereas EfficientNetB3 had precision, sensitivity, and specificity of 89.78%, 94.42%, and 97.28%, respectively. Murugan et al. [4] used a CNN-based DEMNET (dementia network) model in an effort to identify four stages of Alzheimer's disease. The 6400 MRI images that made up the study's dataset were downloaded from Kaggle. Data augmentation was done using the SMOTE approach. Mohammed et al. [5]. Trained AlexNet, ResNet-50, and hybrid models of AlexNet+SVM and ResNet-50+SVM using OASIS and Kaggle MRI datasets. The SMOTE approach was used to balance the groups in an OASIS dataset, whereas data augmentation was used in the Kaggle dataset. After augmentation, AlexNet+SVM outperformed other methods on the Kaggle MRI dataset, achieving an amazing accuracy rate of 94.8%.

To address the problems of early and accurate diagnosis, we proposed a workable alternative in this study (1) A wide range of pre-trained deep convolutional neural networks (CNNs) are extensively experimented with as feature extractors; robust and discriminative deep features are extracted from brain magnetic resonance imaging (MR) and used to identify Alzheimer's disease using softmax classifiers. (2) extensive experimentation done by using hyperparameter tuning optimization on several models of deep convolutional neural networks (CNNs)[46] that have already been trained to increase performance. (3) We also developed an ensemble of different transfer CNN, SETNN (Stacked Ensemble Transferred Neural Network) for the MRI-based detection of Alzheimer's disease to give accurate results. This work presents a novel, very precise method for early Alzheimer's disease identification utilising MRI scans. The suggested model makes use of a method that seeks to achieve greater optimisation during training in comparison to other approaches that have been documented in the literature. This optimization would reduce the computational power required for training, making the model more practical for professionals and scholars. The study model combines deep learning and transfer learning models, results in an excellent level of accuracy that outperforms the functionality of competing alternatives.

2. Materials and Methodology

Numerous designs that may facilitate AD detection and medical image classification have recently been proposed in the literature, as can be seen in the "Literature Review" section. However, because early diagnosis necessitates differentiating between the multiple phases of AD that are now present, it becomes a multiclass classification problem.

2.1. Data Selection

A portion of the Alzheimer's disease Neuroimaging Initiative (ADNI) data, which may be accessed through their database at http://www.loni.ucla.edu/ADNI, was used in this research [16]. MRI datasets were produced by scanning obtained on 1.5T and 3T scanners at different times with a time interval of one to three years. The National Institute of Ageing (NIA), The National Institute of Bioengineering Biomedical Imaging (NIBIB), Independent Pharma Organisation, Food and Drug Administration (FDA), and non-profit organisations collaborated to establish the ADNI initiative in 2003 with a $60 million, five-year agreement [17]. Table 1 presents the specifics of the ADNI1 dataset that we used in our study.

Table 1: Details of ADNI1 dataset, such as the number of individuals, the number of images, descriptive age statistics, the percentage of women in the images compared to men, and the percentage of 1.5 T field strength images compared to 3.0 T images.

Dataset	Subject	Groups	Images	Age(years)				Female (%)	1.5T (%)
				Med	Avg ± Std	Min	Max		
ADNI1	845	All	9149	76.6	76.3 ± 6.9	54.6	93	42.2	82.2
		CN	2701	76.7	77.2 ± 5.1	60	92.8	50.2	80.5
		MCI	4845	76.5	76.0 ± 7.4	54.6	90.9	35.3	83
		AD	1603	76.5	76.1 ± 7.9	55.2	93	49.5	82.5

2.2. MRI Pre-processing

The MRI acquisition data in the ADNI1 dataset contains noise that needs to be addressed before computational analysis [18]. This involves removing noise, normalizing intensity, adjusting contrast, and removing unnecessary background areas. Initial pre-processing techniques, including Grad warp, B1 non-uniformity, and N3 bias field correction [19], were applied to the dataset during capture. To prepare the data for our model, several pre-processing steps were applied, as shown in figure 1. Firstly, spatial normalization was performed to validate the image position. Regardless of differences in subject-to-subject variability in brain size, shape, and microarchitecture, images are processed to verify that the voxels being compared represent the same brain regions. Spatial normalization is the term used to describe the process. The voxels in each brain image are "registered" to represent the same region of the brain during this process. Typically, the images' voxels are registered to the voxels of an accepted "template" brain image. The MANGO toolbox [20] was then used to perform intensity normalisation, noise reduction, correction of bias, adjustments in contrast and rescaling. Each 3D MRI volume contains 256 x 256 x 166 slices, which prevent direct feeding of the data into a 2D-CNN network. Each three-dimensional volume was then rescaled into two-dimensional layers, each with a single channel (axial, coronal, and sagittal) with a size of 300 × 300. Image is rescaled under intensity normalization with the help of following equation (1),

$$I_{new} = (I - MIN)\frac{newMAX - newMIN}{MAX - MIN} + newMIN \quad (1)$$

where I and I_{new} are input and normalized brain images respectively, $newMIN$ $and newMAX$ are the normalised image's intensity ranges (over here they are -1 and 1), and MIN = 0; and MAX = 255 are the input brain image's pixel intensity ranges.

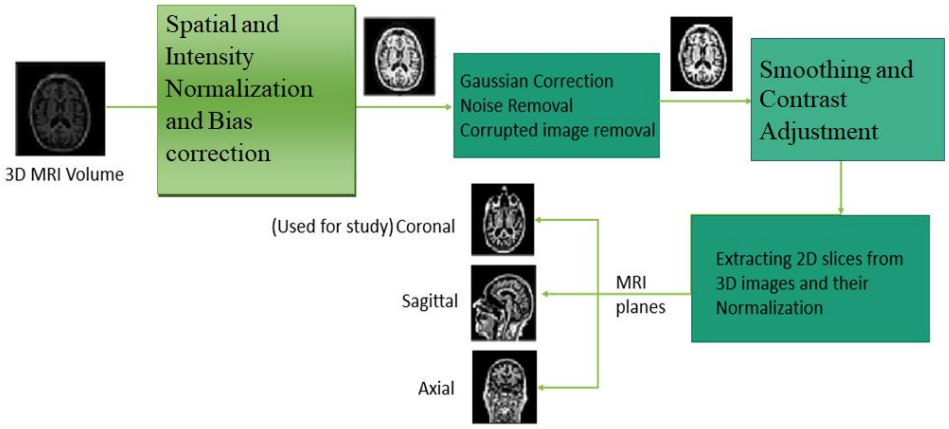

Fig 1: Pre-processing processes summarised

To improve the classification performance of brain MRI images in our datasets, it is necessary to remove undesired spaces and areas through cropping. We use the cropping method, which involves calculation of extreme point [19]. In the beginning the raw MRI data is imported for preprocessing and thresholding is applied to convert the MRI data into a binary, as shown in figure 2. The dilation along with erosion techniques is applied to minimize the noise. The top, bottom, right, and left extreme points of the contour—the longest contour found in the thresholder imagery—are computed. Following that, the image is cropped using the contour and extreme point data. MR images that have been cropped have been resized through bicubic interpolation [21].

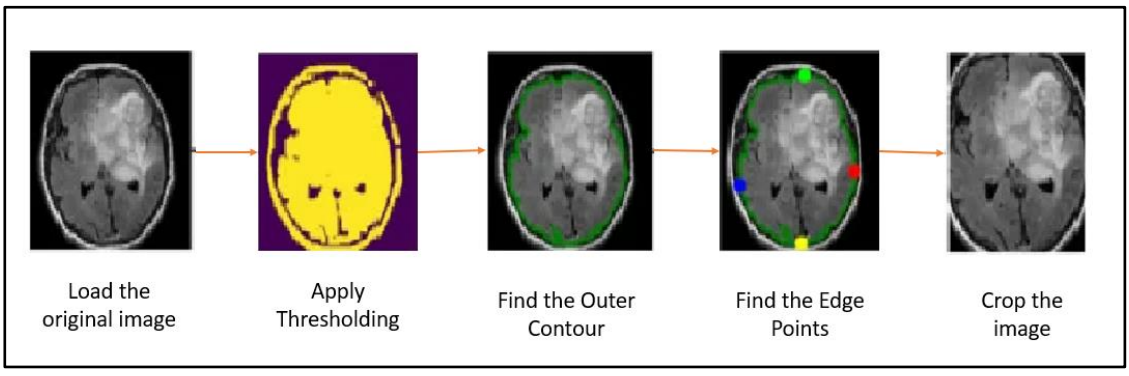

Fig 2: The procedure for cropping the magnetic resonance (MR) image.

To address the limitation of a relatively small MRI dataset, we utilized image augmentation techniques. Image augmentation involves creating an artificial dataset by modifying the original images, which can include variations in scale, rotation, horizontal flipping, brightness, and other factors for generation of new training sets.

2.3. Deep Learning Algorithms (DLAs)

In the context of brain MRI and computer interventions, Convolutional Neural Networks (CNNs) and Deep Learning (DL) are of central importance. Traditional neural networks have developed in Deep Neural Network (DNN) techniques, where the method itself is automatically created without human interaction and the networks' links are determined by data. This characteristic adds to these systems' accuracy and outstanding performance across a range of disciplines. In reality, DLAs are made up of several nerve-based computations which automatically identify characteristics and features in the data and use this information to develop strategies [9].

In a CNN, Neurons are individual features of a convolution layer which are influenced by the pixel density in the surrounding region called the receptive field [12, 16]. The number of convolution operations in a neuron's design boosts its computing efficiency. Convolutional layers, input, hidden units, batch normalisation, and activation techniques are all part of the hierarchical structure of CNNs. Based on the number of layers used, different activation methods and sizes are employed in CNNs; these are empirically discovered by trial and error. If related fields overlap, the entire visible region is covered by the receptive field, or the area of the visual field that CNN neurons only react to changes in [22].

Transfer learning involves transferring weights to a corresponding model from a previously learned network. This approach is crucial for problems where there is a dearth of training data. The network could overfit with insufficient data, which would impede generalisation. The parameters of the transferred network offer proper categorization of moderate quantities of input when the pre-trained model's training dataset is large enough. In the last step, the classifiers of the new model were trained with the expected weights from the pre-trained model [19].

2.4. Proposed Ensemble Model

Our proposed Stacked Ensemble Transfer Neural Networks (SETNN) approach involves stacking method. Here we are considering ensemble of transfer learned models as base models. Three fine-tuned pre-trained models, MobileNetV3,Inception V3, and VGG 16 with CNN using Keras as shown in figure 5 are selected as base models, and then providing output of individual model for the training of meta model which is set to logistic regression. As can be seen in table 3, training time required for Inception V3 and VGG16 is smallest, so we have selected those two models while MobileNetV2 is chosen for its lightweight and fast nature. The top layer of pre-trained model is removed, and output CNN layers are added to extract features in each base model. All models use a learning rate of 0.0001.

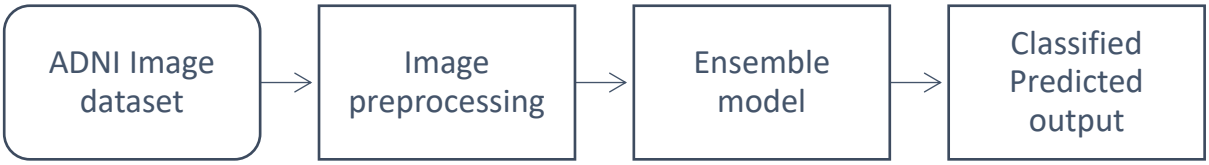

Fig 5: Proposed SETNN model

We have our extensive experiments employing several pre-trained deep convolutional neural networks (CNNs) as feature extractors to extract meaningful and discriminative characteristics from MR images. These features were then used to classify Alzheimer's disease using logistic regression classifiers at meta model level [23]. Additionally, we performed extensive experiments with hyperparameter tuning optimization on various pre-trained CNN models to improve the performance of our strategy. The weight of the model is initialized with the ImageNet weight used in the training of the original model, and we use sparse cross-entropy logarithmic loss function due to the multiclass classification task. Details of hyperparameters are provided in Table 2.

Table 2: Hyper-parameters values for base models

Parameter	Value for SETNN
Input Shape	(32,32,3)
Weight	Initialized to ImageNet
Optimizer	ADAM

Learning Rate	1e-3
Loss Function	Sparse Cross Entropy
Classifier	Softmax
Epochs	5
Batch Size	64
Dropout Rate	0.3

The table 3 displays the average time per epoch (in seconds) for training different pre-trained deep convolutional neural network (CNN) models on non-demented data. The models include popular architectures such as VGG16, VGG19, ResNet50, InceptionV3, InceptionResNetV2, MobileNet, MobileNetV2, DenseNet201, NASNetM, EfficientNetB0, and a custom CNN+MobileNet. The results show that InceptionResNetV2 has the highest average time per epoch at 1102 seconds, while InceptionV3 has the lowest at 298 seconds. These results provide insights into the computational costs associated with training different CNN models on non-demented data, which can be valuable for choosing an appropriate architecture based on time constraints in a specific research or application context [42].

Table 3: Time required for execution

Non-Demented	**Average time per epoch (s)**
VGG16	302
VGG19	348
ResNet50	648
InceptionV3	298
InceptionResNetV2	1102
MobileNet	578
MobileNetV2	582
DenseNet201	894
NASNetM	868
EfficientNetB0	1022
SETNN	590

2.5. Performance Evaluation Metrics

Accuracy (ACC), Precision, sensitivity (SEN), specificity (SPE) and F1 score are some of performance evaluation metrics. True positives (TP) are correctly predicted positive tuples, whereas false positives (FP) are wrongly positive predicted tuples means originally tuples are negative but classified as positive. True negatives (TN) are correctly predicted negative tuples, whereas false negatives (FN) are the positive tuples mislabeled as negative.

Accuracy refers to the classifier's ability to correctly categorise and how each instance will be predicted. You may figure it out using Equation (2)

$$Accuracy = \frac{TP+TN}{TP+TN+FP+FN} \quad (2)$$

Precision is ratio of the number of true positive prediction class values and the total number of positive predictions class values as shown in Equation (3)

$$Precision = \frac{TP}{TP+FP} \quad (3)$$

Recall (sensitivity) is defined as the ratio of number of true positive predictions class to the number of correct predicted class values in the testing dataset. Recall is another term for sensitivity as shown in Equation (4).

$$Sensitivity = \frac{TP}{TP+FN} \quad (4)$$

The specificity is the proportion of true negatives which the algorithm correctly predicted. Apply the following formula to assess specificity:

$$Specificity = \frac{TN}{TN+FP} \quad (5)$$

The F1-score is harmonic mean of a classifier's accuracy and recall as illustrated in equation 6.

$$F1\ score = \frac{2*Precision*Recall}{Precision+Recall} \quad (6)$$

3. Experiments, Results and Discussion

In this part, we present a thorough explanation of the experiment, such as its setup and findings. We begin by discussing the experiment's setup, including the software and hardware parameters used. The outcomes of training and validating the model technique are then reported. The findings from classifiers—Softmax, logistic regression and the individual transfer learned models formed from pre-trained models MobilenetV2, VGG16 and InceptionV3 for extracting features —are discussed in subsection. Finally, we compare the outcomes of our suggested methodology with those of alternative approaches.

The trials were carried out using the Python programming environment provided by the Google Colaboratory Pro platform. Google's cloud offering Colab Pro enables customers to create and run Python programmes on a hosted GPU. To construct our recommended solution, we employed a range of deep learning Python modules such as TensorFlow, Keras, Scikit-learn, Numpy, and OpenCV. In addition, we utilised the Python modules Nibabel, Nilearn, and DeepBrain to interpret MRI neuroimaging results. This work focused on coronal plane visualisation of brain anatomy using the ADNI dataset of MRI images in NIFTI format. The coronal plane, an x-z plane that separates the anterior and posterior, is perpendicular to the ground. According to research, using the coronal plane is more efficient [24].

For our investigation, the dataset was randomly partitioned into two sets: a training set including 80% of the data and a testing set containing 20% of the data. Table 4 displays the performance of 10 pre-trained models as well as the suggested ensemble model SETNN with the two classifiers.

Table 4: Comparative Performance of ten pre-trained model along with proposed ensemble model SETNN with the three classifiers

Pre-trained model Deep Features	**Classifier – Accuracy (%)**			
	SVM (Linear)	**SVM (Non-linear/Sigmoid)**	**SVM(RBF)**	**Softmax (FC)**
VGG16	86.27	86.27	80.39	90.1
VGG19	82.35	82.35	83.78	90
ResNet50	82.35	88.24	90.2	92.1
InceptionV3	90.2	90.2	90.2	93.7
InceptionResNetV2	92.16	92.16	92.16	95.3
MobileNet	86.27	88.24	88.24	89.5
MobileNetV2	87.32	88.69	89.88	90.1
DenseNet201	84.31	88.24	86.27	93.6
NASNetM	84.31	86.27	86.45	91.1
EfficientNetB0	86.23	90.2	92.16	93.3
SETNN	87.2	88.79	90	**99.5**

The suggested SETNN model structure is founded on the stacking of different transfer learned as base models and logistic regression as meta-model reduce overfitting and increase model performance. To normalise the output, batch normalisation layers were added after the final convolution layer and each fully linked layer in every transfer learning model. To reduce overfitting, a dropout layer with a rate of 0.3 was added before the classifier and after the fully connected layer. Pre-trained models were trained using the ADAM optimizer, which has a learning rate of 0.0001. The batch size was set to 64 for the training and validation sets, as well as the number of samples in the testing set. The fixed hyperparameter for model training, called the epoch, was set at 5.

For distinguishing AD and normal MRI imagery, model assessment depends on accuracy and categorical cross-entropy (loss). The amount of data which an algorithm should minimise during training is determined by loss functions. The training and validation curves of SETNN model is shown in Figure 7. The right plots, which span 15 epochs, show accuracy vs. epochs, whereas the left graphs show loss vs. epochs. The training results are shown in red, while the validation results are displayed in orange.

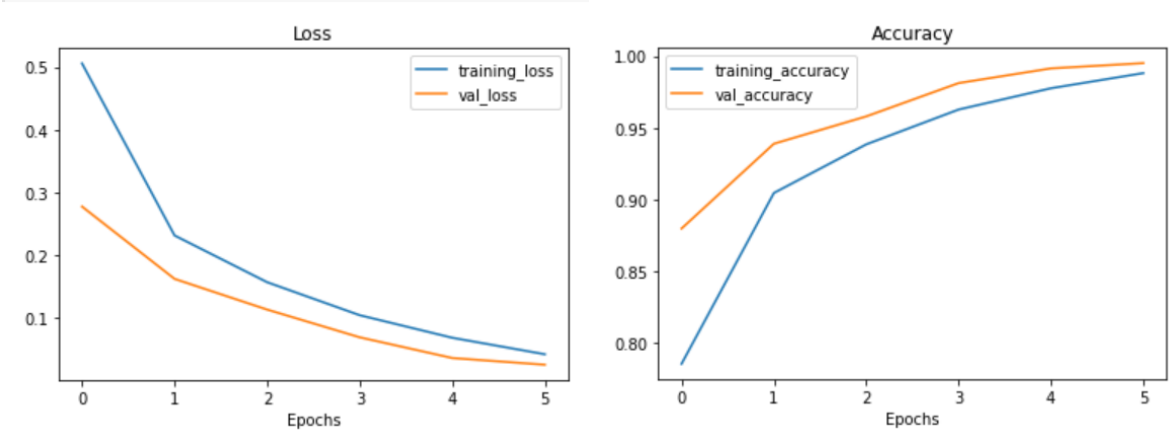

Fig 8: Training and validation performance of SETNN model

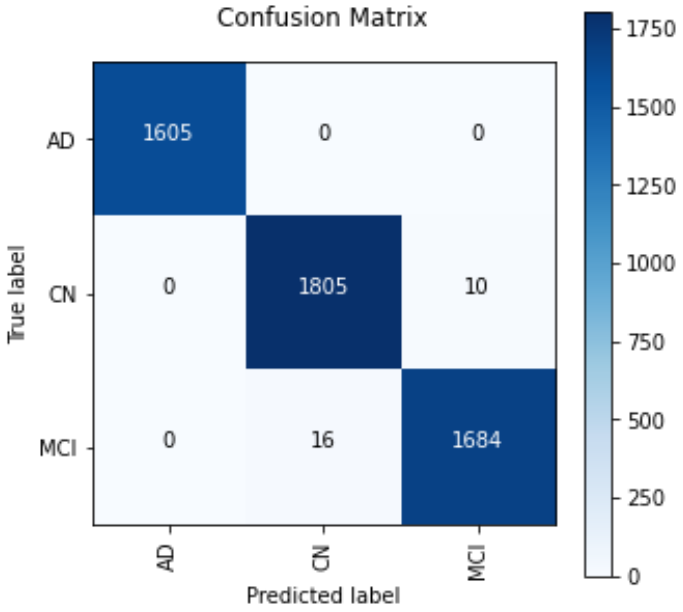

Fig 9: Confusion matrix during testing the SETNN model.

To address our research questions, suggested model's classification performance was assessed using Softmax classifiers on the ADNI dataset [25, 26]. These tests aimed to identify the best precise method for pre-trained AD diagnosis model. In the classifier layer, we initially used Softmax to apply transfer learning to SETNN. The confusion matrix of the Softmax classifier is shown in Figure 8. The prediction results of Softmax are displayed in Table 5 in terms of accuracy, recall, f1-measure, and support, while support is the number of samples.

Table 5: SETNN model experiment results

Data	Precision	Recall	F1-Score	Support
AD	1.0000	1.0000	1.0000	1605.0
CN	0.9912	0.9945	0.9928	1815.0
MCI	0.9941	0.9906	0.9923	1700.0
Accuracy	0.9949	0.9949	0.9949	0.9949
Macro Avg	0.9951	0.9950	0.9950	5120.0
Weighted Avg	0.9949	0.9949	0.9949	5120.0

Tables 5 and 6 show that the recommended AD diagnostic model was successful, with a high AD classification accuracy (99.49%). The findings show that Softmax classifiers have the greatest accuracy among them. Furthermore, the SVM using RBF kernel ranks as the second-best classifier.

Table 6: Proposed model test performance with state-of-the-art existing methods

References	Feature Extraction	Classifier	Accuracy
Loddo et al. [1]	Inception-ResNet-v2	Softmax	98.51% in the binary case, and 98.67% in the multiclass case
Mahendran et al. [2]	EDRNN	Softmax	88.7%
Sava [3]	EfficientNetB0	Softmax	92.98%
Murugan et al. [4]	DEMNET	Softmax	95.23%.
Mohammed et al. [5]	AlexNet+SVM	Softmax	98.3%
Gharaibeh et al. [6]	InceptionV3 and DenseNet201	Softmax	99%
Basher et al. [7]	CNN and DNN	Softmax	94.82% and 94.02% for left and right hippocampi respectively
Proposed Model	**SETNN**	**Softmax**	**99.49%**

4. Conclusion and Future

Alzheimer's disease symptoms grow gradually over time, and there is presently no treatment. Existing treatment options for Alzheimer's disease can only delay the course of symptoms, therefore early detection is crucial. To enhance early diagnosis, a deep learning-based classification model with an integrated feature selection strategy was used to categorise Alzheimer's patients. The ADNI dataset was used for the analysis. Prior to feature selection, the data was pre-processed, including quality checking, normalisation, and augmentation. Ten pre-trained feature selection approaches were evaluated based on the relevance of feature extraction and the best technique was picked for the suggested ensemble classification model. The implementation of an SETNN and comparisons of its results with other models were conducted. The findings showed that, when compared to previous approaches, the suggested model's classification accuracy had significantly improved.

Deep learning-based AD research is continuously being developed for improved performance and transparency. Studies on detecting Alzheimer's disease using deep learning is shifting away from hybrid methods and towards a model that simply employs deep learning algorithms. However, strategies must be developed to incorporate completely different types of data in a deep learning network.

Availability of data and materials

Alzheimer's Disease Neuroimaging Initiative (ADNI) data available on http://www.loni.ucla.edu/ADNI [11].

References

[1] Loddo, A., Buttau, S., & Di Ruberto, C. (2022). Deep learning based pipelines for Alzheimer's disease diagnosis: A comparative study and a novel deep-ensemble method. Computers in Biology and Medicine, 141, 1-15.

[2] Mahendran, N., & PM, D. R. V. (2022). A deep learning framework with an embedded-based feature selection approach for the early detection of Alzheimer's disease. Computers in Biology and Medicine, 141(September 2021).

[3] Sava¸s, S. (2022). Detecting the stages of Alzheimer's disease with pre-trained deep learning architectures. Arabian Journal for Science and Engineering, 47(2), 2201-2218.

[4] Murugan, S., Venkatesan, C., Sumithra, M. G., Gao, X. Z., Elakkiya, B., et al. (2021). DEMNET: A deep learning model for early diagnosis of Alzheimer diseases and dementia from MR images. IEEE Access, 9, 90319-90329.

[5] Mohammed, B. A., Senan, E. M., Rassem, T. H., Makbol, N. M., Alanazi, A. A., et al. (2021). Multi-method analysis of medical records and MRI images for early diagnosis of dementia and Alzheimer's disease based on deep learning and hybrid methods. Electronics, 10, 1-20.

[6] Gharaibeh, M., Almahmoud, M., Ali, M. Z., Al-Badarneh, A., El-Heis, M., et al. (2022). Early diagnosis of Alzheimer's disease using cerebral catheter angiogram neuroimaging: A novel model based on deep learning approaches. Big Data and Cognitive Computing, 6(2), 1-23.

[7] Basher, A., Kim, B. C., Lee, K. H., & Jung, H. Y. (2021). Volumetric feature-based Alzheimer's disease diagnosis from sMRI data using a convolutional neural network and a deep neural network. IEEE Access, 9, 29870-29882.

[8] Mirzaei, G., & Adeli, H. (2022). Machine learning techniques for diagnosis of Alzheimer disease, mild cognitive disorder, and other types of dementia. Biomedical Signal Processing and Control, 72.

[9] Dadar, M., Pascoal, T. A., Manitsirikul, S., Misquitta, K., Fonov, V. S., et al. (2017). Validation of a regression technique for segmentation of white matter hyperintensities in Alzheimer's disease. IEEE Transactions on Medical Imaging, 36(8), 1758-1768.

[10] Lei, B., Liang, E., Yang, M., Yang, P., Zhou, F., et al. (2022). Predicting clinical scores for Alzheimer's disease based on joint and deep learning. Expert Systems with Applications, 187.

[11] Islam, J., & Zhang, Y. (2018). Early diagnosis of Alzheimer's disease: A neuroimaging study with deep learning architectures. In IEEE Conf. on Computer Vision and Pattern Recognition Workshops, Salt Lake City, USA, pp. 1994-1996.

[12] Ninni Persson, Paolo Ghisletta, Cheryl L. Dahle, Andrew R. Bender, Yiqin Yang, Peng Yuan, Ana M. Daugherty, Naftali Raz, Regional brain shrinkage and change in cognitive performance over two years: The bidirectional influences of the brain and cognitive reserve factors, NeuroImage, Volume 126, 2016, Pages 15-26, ISSN 1053-8119, https://doi.org/10.1016/j.neuroimage.2015.11.028.

[13] Sheng, J., Xin, Y., Zhang, Q. et al. Predictive classification of Alzheimer's disease using brain imaging and genetic data. Sci Rep 12, 2405 (2022). https://doi.org/10.1038/s41598-022-06444-9.

[14] Ding, X., Yang, Y., Steinbach, M., & Fujimoto, K. (2019). Hierarchical 3D deep convolutional neural networks for segmenting layered tubular structures in 3D images. IEEE Transactions on Medical Imaging, 38(1), 116-126.

[15] Padilla, P., Lopez, M., Gorriz, J. M., Ramirez, J., Salas-Gonzalez, D., et al. "NMF-SVM based CAD tool applied to functional brain images for the diagnosis of Alzheimer's disease." IEEE Transactions on Medical Imaging, vol. 31, no. 2, 2012, pp. 207-216.

[16] Mueller, S. G., Weiner, M. W., Thal, L. J., Petersen, R. C., Jack, C. R., Jagust, W., et al. (2005). Ways toward an early diagnosis in Alzheimer's disease: The Alzheimer's disease neuroimaging initiative (ADNI). Alzheimer's Dement., 1, 55-66.

[17] Ho AJ, Hua X, Lee S, Leow AD, Yanovsky I, Gutman B, Dinov ID, Leporé N, Stein JL, Toga AW, Jack CR Jr, Bernstein MA, Reiman EM, Harvey DJ, Kornak J, Schuff N, Alexander GE, Weiner MW, Thompson PM; Alzheimer's Disease Neuroimaging Initiative. Comparing 3 T and 1.5 T MRI for tracking Alzheimer's disease progression with tensor-based morphometry. Hum Brain Mapp. 2010 Apr;31(4):499-514. doi: 10.1002/hbm.20882. PMID: 19780044; PMCID: PMC2875376.

[18] Gao, J., Jiang, Q., Zhou, B., & Chen, D. "Convolutional neural networks for computer-aided detection or diagnosis in medical image analysis: An overview." Mathematical Biosciences and Engineering, vol. 16, no. 6, 2019, pp. 6536-6561.

[19] Park, M.; Moon, W.J.; Structural, M.R. Imaging in the Diagnosis of Alzheimer's Disease and Other Neurodegenerative Dementia: Current Imaging Approach and Future Perspectives. Korean J. Radiol. 2016, 17, 827–845

[20] Research Imaging Institute — Mango (mangoviewer.com)

[21] Douglas W. Scharre, MD, Preclinical,Prodronal and Dementia Sages of Alzheimer's Disease, Practical Neurology, June 2019

[22] Cecotti, H., & Graeser, A. "Convolutional neural network with embedded Fourier transform for E.E.G. classification." Proceedings of the 19th International Conference on Pattern Recognition, 2008, pp. 1-14.

[23] Feng, Q., Chen, W., Zheng, P., & Yu, H. (2019). A novel Alzheimer's disease detection model with deep convolutional neural networks. Frontiers in Neuroscience, 13, 509.

[24] Rezaei, M., Alipoor, M., &Sahraian, M. A. (2019). MRI-based radiomics for Alzheimer's disease prediction: A systematic review. Journal of Alzheimer's Disease, 72(3), 771-786

[25] Balachandar, R., Ahmad, S., Sharmila, S., & Begum, S. (2019). Detecting Alzheimer's disease using 3D convolutional neural network with MRI images. Informatics in Medicine Unlocked, 15, 100188.

[26] Kwon, D., Akbari, H., Da, X., Gaonkar, B., & Davatzikos, C. "Multimodal brain tumor image segmentation using GLISTR." Proceedings of the BRATS-MICCAI (2014), 2014, pp. 18-19.

[27] Hosseini-Asl, E., Hajian-Tilaki, K., & Mahmoudi-Nezhad, G. S. (2020). Radiomics-based classification of Alzheimer's disease and mild cognitive impairment from structural MRI. Journal of Neuroscience Methods, 348, 108977.