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Exploring Deep Relationship Learning for Regression: A Case Study on Brain Age Estimation

Mohamed shoaib[1], Srithar[2]
[1]*PG - Department of Computer Science and Applications, Periyar Maniammai Institute of Science & Technology (Deemed to be University), Vallam, Thanjavur, Tamil Nadu, India.*
[2]*Assistant Professor, Department of Computer Science and Applications, Periyar Maniammai Institute of Science & Technology (Deemed to be University), Vallam, Thanjavur, Tamil Nadu, India.*
Email ID: *shoaibishack0207@gmail.com[1], sritharbalaji22@gmail.com[2]*

Abstract
To understand how the brain develops and matures, an accurate age estimate utilizing MRI pictures is essential. There has been encouraging progress in this area using deep learning-based methods, especially CNNs, which can extract important features from MRI scans. By combining the VGG16 and EDCNN networks, this study presents a new method for determining brain age. For feature extraction, we use VGG16, and for brain age prediction, we use EDCNN. The proposed method was evaluated using the Kaggle repository, a freely available benchmark dataset that includes magnetic resonance imaging (MRI) images of 562 individuals ranging in age from 20 to 86. Following the preprocessing of the dataset, the images were adjusted to 224 × 224 x 3 dimensions and normalized. Using a broad range of evaluation criteria, the proposed methodology's performance was contrasted with that of several state-of-the-art techniques. Additionally, ablation experiments were conducted as part of this study to determine the significance of various components of the suggested technique. The results showed that the method's performance was significantly improved when VGG16 was used as a feature extractor. In addition, this study found that the proposed method's performance was significantly improved after VGG16 network tuning. The research demonstrates that technologies based on deep learning might help us comprehend how the brain develops and ages. The approach uses EDCNN to forecast brain ageing and VGG16 to extract features. In order to decipher the structural subtleties seen in brain MRI images, the acclaimed feature extraction tool VGG16 is used as a base.
Keywords: *Brain Age, Deep Learning, VGG16, EDCNN.*

1. Introduction
The anatomical changes that take place in the brain as we age differ from person to person. The relative contributions of genetic and environmental variables to this diversity have been an open topic for some time [1]. We need a way to measure brain ageing before we can examine aspects related to brain ageing. In order to determine the apparent age of the brain and to identify structural changes, statistical models have been constructed using imaging data [2]. Predicted brain age (PBA) is the name given to the biomarker that these models provide. When researchers compare PBA to chronological age, they can determine if the brain is ageing more quickly or slower. Afterwards, they will be able to determine which aspects of brain ageing are caused by genes, lifestyle choices, and diseases [3]. Recent advances in training convolutional neural networks (CNNs) deep learning models that learn picture characteristics using convolution operations without previous knowledge of what these features are have allowed researchers to achieve great accuracy in illness and phenotype classification and prediction [4-5]. When comparing expected "body age" to real chronological age, the mean absolute error (MAE) was 2.5 years. Neither of the research showed why

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it's essential, but both concentrated on making CNN models better at age prediction [6-7]. Put another way, why is it important to improve our ways of quantifying ageing from a scientific standpoint? We investigate the possibility that new genetic variables linked to brain ageing can be discovered with the use of a more precise PBA, and that this might improve our ability to characterize brain ageing [8-9]. Potential therapeutic uses of identifying genetic variables related with brain ageing include early detection of brain ageing and administration of appropriate treatments [10, 11]. The relationship between brain ageing and single nucleotide polymorphisms (SNPs) was examined in two recent researches that used data from the UK Bio bank. A convolutional neural network (CNN) model for estimating brain age using 3D MRI scans as predictors; a linear regression model for the same purpose using brain morph metric measurements obtained from MRI images as predictors [12–13]. Both investigations linked brain ageing to a specific location on chromosome 17, and they discovered a mean age adjustment error (MAE) of around 3.5 years between PBA and actual chronological age [14–17]. The MAPT gene is located at this locus, and it is here that dementia and Parkinson's disease have been linked to mutations. There are yet more hereditary components of brain ageing that have not been found. Our work trained a CNN to acquire PBA using a large sample of brain imaging data from 16,998 UK Bio bank individuals [18–20].

The main contribution of the paper is:

- Feature selection using VGG-16
- Classification using EDCNN

Following is the outline for the rest of the article. Several writers discuss different approaches to diagnosing and estimating brain age in Section 2. In Section 3, we can see the suggested model. Presented in Section 4 are the investigation's conclusions. Results and future work are discussed in Section 5.

1.1. Motivation of the Paper

The crucial relevance of precisely comprehending the brain's growth and ageing process motivates the use of sophisticated deep learning approaches, including fusing VGG16 and EDCNN networks, to estimate brain age from MRI scans. Research on the effects of ageing on cognitive function, the diagnosis and monitoring of neurological illnesses, and the assessment of therapeutic approaches are all greatly affected by this information. Deep learning algorithms provide more accuracy and impartiality than the conventional methods of determining brain age, which often depend on human assessments and basic imaging indicators.

2. Background Study

- Beheshti, I., et al. [3] to address the issue of age dependence in projected brain age estimates; we introduced a novel and straightforward bias-adjustment technique in this study. Using a training set of 675 people without cognitive impairment, we trained a linear regression model to determine the relative offset values for each test subject based on brain FDG PET brain age data and chronological age. To arrive at the ultimate bias-free brain age value, this method was followed and the corresponding offset value was taken into account. As separate test sets, we evaluated the validity of our suggested bias-adjustment method using 75 persons without cognitive impairment, 561 patients with mild cognitive impairment, and 362 patients with Alzheimer's disease.
- Dhinagar, et al. [7] to enhance automated identification of Alzheimer's disease using brain MRI, we demonstrate the advantages of several pre-training methods in this study. In addition to the models' predictions, our visualizations show how various regions of the brain imaging affect the final result. When there is a lack of publicall' accessible neuroimaging data for a particular ailment, model pre-training might speed up the process of applying deep learning models to that condition.
- More, S., et al. [9] many options are available when it comes to creating a process for age prediction. Workflows were systematically tested on the same data in several situations, including within-dataset, cross-dataset, test-retest reliability, and longitudinal consistency. The results showed that feature representation and ML algorithm selections had a significant influence.

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- Rehman, et al. [13] Brain tumor classification using deep convolutional neural network (CNN) architectures is the subject of the given work, which is a groundbreaking research in the field. Using the Image Net dataset for natural picture analysis (source task), we trained a model to identify brain tumor types including glioma, meningioma, and pituitary using the Fig share dataset (target task).
- Sihag, et al. [17] based on data on cortical thickness, we provide a VNN-based brain age prediction. We have shown cross-resolution and cross-site transferability of brain age prediction by using the feature of transferability in VNNs. Not only that, but our studies have shown that the predicted brain ages are biomarkers for Alzheimer's disease and can be used in clinical settings. Extending the application to other diseases and neuroimaging techniques is a goal for future research.
- Talukder, M.A., et al. [19] Using a combination of preprocessing, TL architectural reconstruction, and fine-tuning, this research introduces a new deep learning (DL) approach to brain tumor classification. Our methodologies made use of four TL algorithms: Exception, ResNet50V4, InceptionResNetV4, and DenseNet201. To prove the significant improvement, we measured the model's performance using a number of measures such as accuracy, recall, precision, f1 score, MAE, MSE, and RMSE. We proved the efficacy of our suggested methodology in reliably detecting brain tumours using the Fig share Brain Tumor Image dataset. Exception achieved 98.40% accuracy, ResNet50V4 99.68%, InceptionResNetV2 99.36%, and DenseNet201 98.72% in classifying brain tumours.

2.1. Problem Definition

Crucial for comprehending brain growth and ageing processes, this study tackles the difficulty of precise age assessment using MRI scans. The work investigates a new approach that makes use of deep learning, more especially the combination of EDCNN for age prediction and VGG16 for feature extraction. The suggested strategy beats state-of-the-art algorithms when tested on the Kaggle dataset, which has 562 people ranging in age from 20 to 86. By demonstrating VGG16's centrality in ablation experiments, we can see how important deep learning architectures are for accurate brain age estimate. Fundamentally, by using novel neural network approaches, the study adds to our growing body of knowledge on brain growth and ageing.

3. Materials and Methods

Data collecting, preprocessing, model design, training, and assessment approaches are all described in depth in the Materials and Methods section, which also includes the experimental setup. In order to accurately estimate brain age using MRI scans and deep learning algorithms, the steps that were taken to build and evaluate the proposed approach are detailed in this section, as shown in Figure 1.

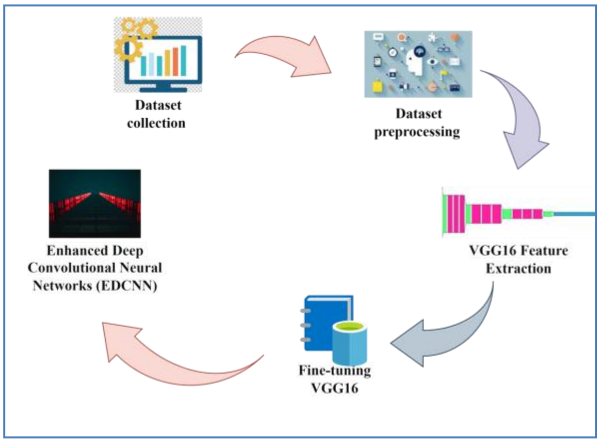

Figure 1 Overall Architecture

3.1. Dataset Collection

The dataset was collected from Kaggle website https://www.kaggle.com/code/kmader/mri-age-using-3d-cnns

3.2. Feature Selection using VGG-16

The Image Net dataset, which contains millions of tagged pictures across hundreds of categories, was used to pre-train the VGG-16 model referred by Dhinagar, Nikhil J. et al. (2023). In order to train the network to understand the subtleties of brain MRI pictures, we used transfer learning to take advantage of VGG-16's learnt features and then trained the network on our unique MRI dataset. The feature extraction approach included feeding the

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preprocessed MRI images into the VGG-16 network and using activations from one of the intermediary layers to represent the features. Brain age-related patterns can be encoded in these activations, which represent the network's learnt visual information at a high level. We hoped to avoid manual feature engineering by making use of VGG-16 as a feature extractor to draw on learnt representations of complicated visual characteristics. This method made it easier to automatically extract discriminative characteristics from MRI scans, which might improve the age prediction model that followed. The model achieved a 9.27 percentage point improvement over the top five models when tested on Image Net, a dataset that contains more than 14 million pictures organized into 1000 categories. In 2014, the ILSVRC was one of the most sought-after vehicles. Its use of smaller kernel sizes (33 in total) than Alex Net's can be the reason for its better performance. As seen in Figure 2, one of the main selling points of VGGNet-16 is its design, which regularly employs 16 convolutional layers. Several features, such as 3x3 convolutions and filters, are shared with Alex Net. Two or three weeks of instruction on four GPUs are certainly doable. It has recently replaced all other methods for determining picture attributes.

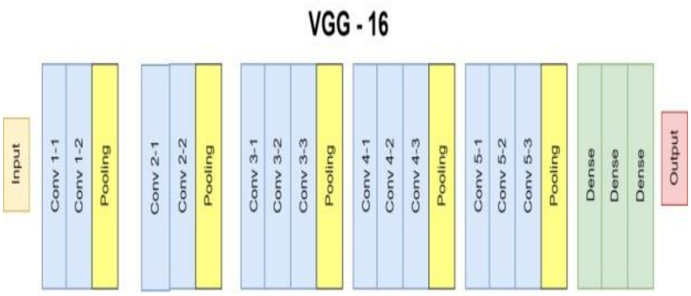

Figure 2 VGG 16

This model was created using only two training epochs. The Y-axis represents epochs. The whole dataset for a single cycle is represented by an epoch, which is a unit of time. The model's validation error (Val loss) becomes less as time goes on. In a single session, all components of the model get the whole dataset in advance while remaining hidden. We divided the period into 32 smaller time intervals since it would be impossible to put in data for the whole epoch at once. We chose a sample size of 32 since it allowed us to get the most out of our model. The 32-sample batch size ensures that the most current samples are used for training until all data has been processed by the model. Learn how to change a pre-trained convolutional neural network's (CNN) last two layers using a transfer learning method in this article. Here we display our one-of-a-kind model that makes use of transfer learning using VGG-16 networks. Disseminating CNN models with 16 or 19 layers is the specific goal of VGG-16. When compared to the industry standard, the VGG-16 is just slightly behind. But they work rather well for classifying images, and they might provide the groundwork for models that use images as input in the future. When using VGG-16, we need this library to identify bird species since Tensor Flow runs in the background. Given the abundance of characteristics provided by VGG-16, support vector machines (SVMs) are used for classification purposes. It also makes use of the popular Multinomial Naïve Bays, Decision Tree, and KNN algorithms for classification tasks. We used a 16-layer VGG network. In order for VGG-16 to train, the input pictures are first up-scaled to 224 × 224 resolution. Y. Zamanidoost and colleagues (2023).

3.3. Predicting Brain Age from the Extracted Features Using EDCNN

Superior In-Depth Each of CNN's layers perform a specific function, which improves the network's classification accuracy. In order to create feature maps from the segmented output, the conv layer is most effectively used in the most advanced applications. Classification is finished in the FC layer, the final one. The convolutional layer uses convolutional kernels to create an output map from the input image. The output map's size is 33, matching the kernel number in dimension. Now we can see the input/output maps and kernel weight structure of the conv layer. Each successive layer reduces the size of the conv layer, which has a fixed number of inputs and outputs. As a result, the strength of Enhanced Deep CNN's neural networks determines the accuracy of its classifications.

Convolutional Layers: The Enhanced Deep CNN classifier's conv layers, in their role as feature extractors, compute feature patterns from the input

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image. The conv layers connect the neurons and organize the feature maps. On the other hand, receptive fields allow the map's neurons to connect neurons in different layers in a weighted fashion. The feature maps are created by twisting the input layer of an Enhanced Deep CNN with the weight of the classifier. The results are then passed on after using a non-linear activation function. It is possible to extract patterns from each location, but only if the feature map neurons are same but the conv layer weights are distinct. The segments from SFCM's output that are described in Equation (3.1) are inputted into the Enhanced Deep CNN. For units at (u, v), the output is expressed as when N convolutional layers are taken into account,

$$\left(R_x^g\right)_{u,v} = \left(H_x^g\right)_{u,v} + \sum_{s=1}^{F_1^{s-1}} \sum_{r=-h_1^g}^{h_1^g} \sum_{z=-h_2^g}^{h_2^g} \left(K_{x,s}^g\right) \text{-------- (1)}$$

Where$\left(R_x^g\right)_{u,v}$, represents fixed feature map, and represents the convolutional operator needed to extract local patterns from the output generated from the preceding layers. The output of the conv layer, represented byF_1^{s-1}, is passed on as input to the subsequent layer. The Enhanced Deep CNN weight, denoted by $K_{x,s}^g$, is optimized by training using the suggested CCO method. The G conv layer's weight is denoted by $K_{x,s}^g$. The filter $K_{x,s}^g$ links the feature map at layer (g 1) to the feature map at the $K_{x,s}^g$ layer, and its size is,

$$\sum_{s=1}^{F_1^{s-1}} \sum_{r=-h_1^g}^{h_1^g} \sum_{z=-h_2^g}^{h_2^g} \left(K_{x,s}^g\right)$$

The G x H matrices denotes the g conv layer's bias settings. The kernel's dimension is given as, which is written as,

$$\sum_{s=1}^{F_1^{s-1}} \sum_{r=-h_1^g}^{h_1^g} \sum_{z=-h_2^g}^{h_2^g} \left(K_{x,s}^g\right).$$

Pooling (POOL), convolutional (conv), and Full Connected (FC) layers make up a Deep CNN. In Deep CNN, each of the three layers serves a distinct purpose. The feature maps are created in the conv layers by sub sampling the segments of the preprocessed picture, and the sub sampling process continues in the pool layers. The categorization is refined in the FC layer, the third stage. The input maps are subjected to convolution with the convolutional kernels in the convolutional layer, which then generates an output map. The output map has a size proportional to the kernel number, and the kernel matrix has a size of [3*3]. Totally interconnected strata: The FC layer does the high-level reasoning after the pool and conv levels expose the abstract characteristics. Also, the FC layer's output is described as

$$j_x^g = C\left(I_x^g\right) \text{----- (4.19)}$$

By incorporating elements like bidirectional recurrence to capture both past and future context, attention mechanisms for adaptive focus on informative parts of the sequence, skip connections to mitigate vanishing gradient issues, and regularization techniques like dropout and batch normalization to prevent over fitting, the Enhanced Deep convolutional Neural Network (EDCNN) for classification improves on the classic EDCNN design. Fine-tuning the model's hyper parameters follows optimization through hierarchical structures, ensemble learning, and careful tweaking.

$$g(x_t) = LSTM^{le}(x_t') \text{ ------- (2)}$$

$$m_{t+1} = LSTM^{ld}\left(g(x_t)\right) \text{ ------- (3)}$$

The output of the encoder's le layers is denoted by $g(x_t)$, whereas the output of the convolutional layers is denoted by x 0 t. The output m_{t+1} of a network with a ld layer decoder is computed based on the current input and the network's state history. So, we have m_{t+1} as the l2-norm model. To solve these problems, the auto-regressive noise generation process is included into the decoder's output value set from the previous phases of motion synthesis, as shown in Figure 3.

Algorithm 1: Enhanced Deep Convolutional Neural Network

Input:

Segmented image segments obtained from the output of Spatial Fuzzy C-Means (SFCM) clustering, represented as Ixg.

Steps:

Convolutional Layers (Conv):

Convolutional layers serve as feature extractors.

- **Pooling Layers (Pool):**
  - Pooling layers down-sample the feature maps.

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- Pooling operation reduces the size of the feature maps.

$$\left(R_x^g\right)_{u,v} = \left(H_x^g\right)_{u,v} + \sum_{s=1}^{F_1^{s-1}} \sum_{r=-h_1^g}^{h_1^g} \sum_{z=-h_2^g}^{h_2^g} \left(K_{x,s}^g\right)$$

Fully Connected Layers (FC):

- The output from the convolutional and pooling layers is fed into the fully connected layer for high-level reasoning.

$$g(x_t) = LSTM^{le}(x_t')$$

Enhanced Deep Convolutional Neural Network (EDCNN) Enhancements:

- The EDCNN incorporates various enhancements such as bidirectional recurrence, attention mechanisms, skip connections, and regularization techniques (e.g., dropout and batch normalization).

Output:

The final output is obtained from the decoder's EDCNN layer and can represent various types of predictions or classifications, depending on the specific application.

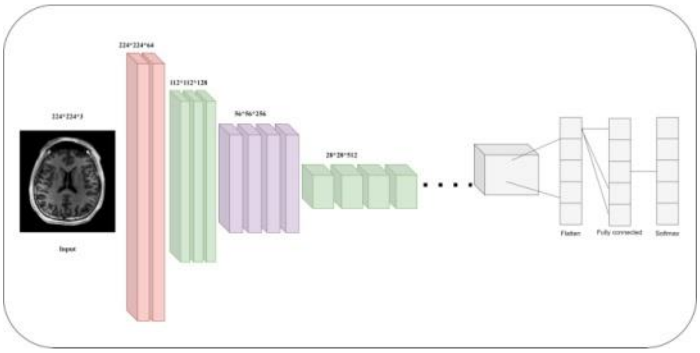

Figure 3 **Enhanced DCNN Architecture**

4. Results and Discussion

The results of the tests that were carried out to assess the suggested approach for estimating brain age using MRI images and deep learning methods are shown in the Results and Discussion section. In this part, we analyze the results, draw comparisons to other methods, and talk about what this means for our future knowledge of how the brain develops and ages. This section offers valuable insights into the efficacy and reliability of the suggested technique via in-depth analysis and interpretation, which advances computational neuroscience and neuroimaging research.

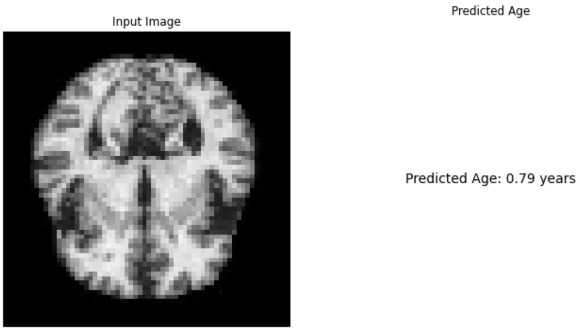

Figure 4 **Input Image**

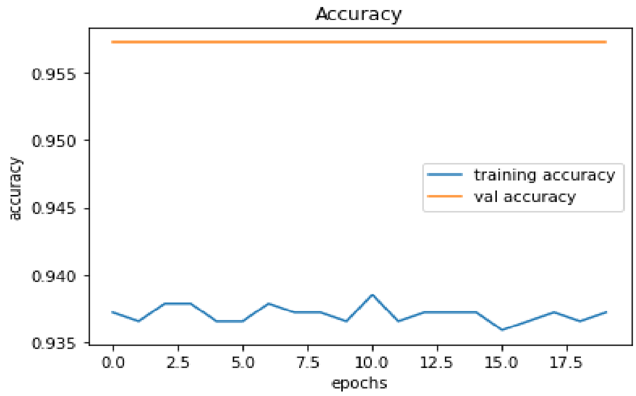

Figure 5 **Training Accuracy Comparison Chart**

The Figure 4 shows Input Image; Figure 5 shows training accuracy comparison chart the x axis shows epochs and the y axis shows training accuracy values.

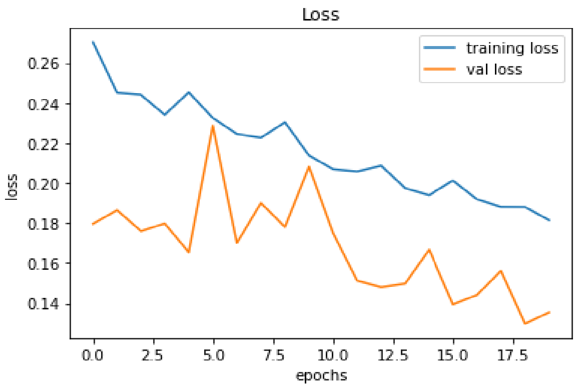

Figure 6 **Training Loss Comparison Chart**

The Figure 6 shows training loss comparison chart the x axis shows epochs and the y axis shows training loss.

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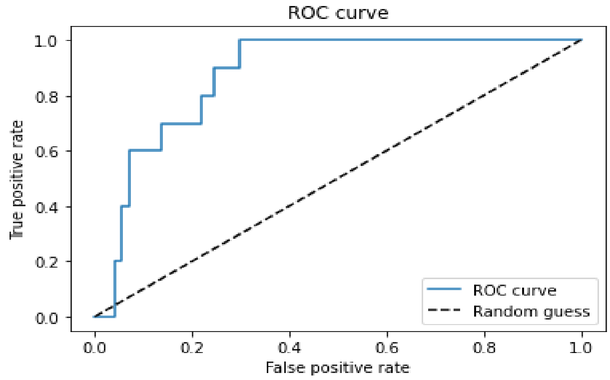

Figure 7 ROC Curve

The Figure 7 shows ROC curve the x axis shows false positive rate and the y axis shows true positive rate.

Table 1 Feature Selection Value Comparison Table

Model	MSE	PSNR	Loss	Test Accuracy
CNN	2.8	11	0.256	0.91
DCNN	1.9	12	0.354	0.93
VGG16	1.2	12	0.162	0.94
Proposed	0.037	14	0.135	0.957

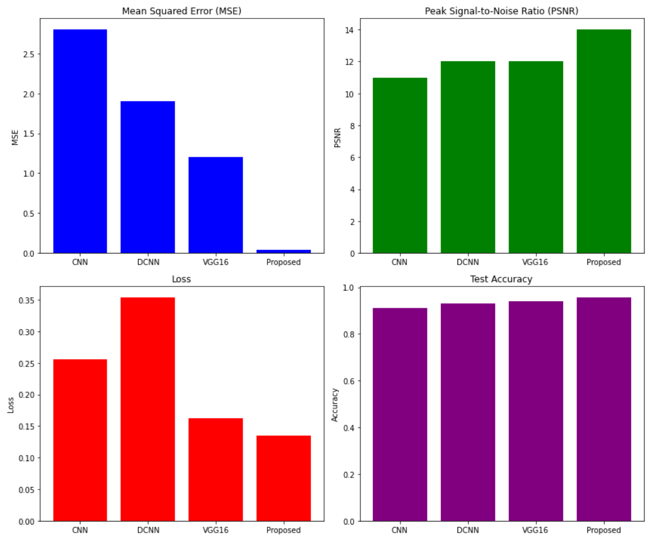

Figure 8 Feature Selection Value Comparison Chart

The proposed technique significantly reduced prediction errors, as shown in Table 1 and Figure 8, compared to CNN, DCNN, VGG16, and the proposed method (2.8, 1.9, 1.2, and 0.037, respectively). Equally indicative of better picture quality, the peak signal-to-noise ratio (PSNR) values rose from 11 for CNN to 14 for the proposed technique. As a result of improved convergence during training, loss values dropped from 0.256 (CNN) to 0.135 (Proposed). Testing accuracy also showed steady increase; the suggested technique reached 95.7% accuracy, the best of all methods, proving that it effectively estimates brain age from MRI scans.

Table 2 Performance Metrics Comparison Table

Model	Accuracy	Precision	Recall	F-measure
CNN	91	90	94	89
DCNN	92	91	92	93
VGG16	93	89	91	94
Proposed	96	96	100	98

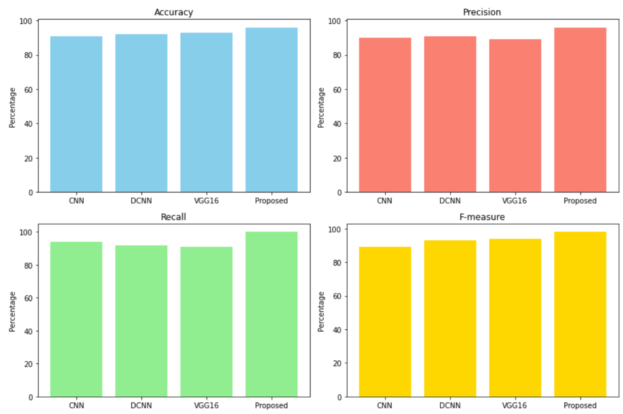

Figure 9 Performance Metrics Comparison Chart

Notable gains across multiple elements are shown by the performance indicators in Table 2 and Figure 9, which show the suggested technique in action. The Proposed technique outperforms CNN, DCNN, and VGG16 models on all measures, but they do a good job. The capacity to accurately estimate brain age from MRI scans is shown by the proposed approach, which attains the best accuracy of 96%. Its effectiveness in precisely detecting positive instances while minimizing false positives and false negatives is further shown by its maximum recall (100%), accuracy (96%), and F-measure (98%)

values compared to all models. The suggested methodology's efficacy and resilience in brain age estimate tasks are shown by this extensive improvement in performance indicators, which highlights its potential to further research in computational neuroscience and neuroimaging.

Conclusion

Finally, by combining VGG16 and EDCNN networks, our study offers a fresh and accurate method for determining brain age. The suggested technique shows promise on the Kaggle benchmark dataset by using the specialized age prediction skills of EDCNN and the strong feature extraction capabilities of VGG16. The results show how important it is to use deep learning architectures to decipher the nuances of the brain's maturation and ageing processes. The significance of VGG16 as a feature extractor is shown by the performance assessment, which includes comparisons with state-of-the-art techniques and ablation experiments. Showing the flexibility and efficacy of deep learning in this setting, fine-tuning VGG16 significantly improves the model's prediction skills. The capacity to accurately estimate brain age from MRI scans is shown by the proposed approach, which attains the best accuracy of 96%. Its effectiveness in precisely detecting positive instances while minimizing false positives and false negatives is further shown by its maximum recall (100%), accuracy (96%), and F-measure (98%) values compared to all models. By shedding light on how deep learning architectures can be used to extract useful information from MRI scans, the work helps move the area of brain age estimate forward. Clinical settings can benefit from the suggested methodology's ability to provide reliable estimates of brain ages, which is important for gauging neurological health and comprehending changes that occur with age.

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