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BAENet: A Deep Learning Framework with Enhanced Convolutional Neural Network for Brain Age Estimation

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Abstract

The assessment of brain age has specific applications like finding whether the aging pattern looks like healthy brain or it is affected by some element. Since brain is very important organ that controls human functionality, it is useful to know its aging patterns. The development of artificial intelligence, such as deep learning, has made it feasible to analyze brain MRI pictures and identify problems in the brain. There are many existing research endeavours to estimate brain age of individuals. The deep learning model like convolutional neural network is widely used in medical image processing. However, from the literature, it was observed that there is need for architecture resilience for improving age estimation process. Towards this end we proposed a deep learning framework that helps in automatic estimation of brain age. We also proposed a novel deep learning model and named it as Brain Age Estimation Network (BAENet). This model is based on CNN. The proposed model Has increased learning capabilities in solving the problem of brain age estimation. The model has more number of layers for progressively learning the brain modality for leveraging performance. The Learning based Brain Age Estimation (LbBAE) algorithm is what we suggested. A benchmark data set known as UK Biobank is used for our empirical study. The outcomes of the experiment showed that the suggested model outperformed ResNet50 with least Mean Absolute Error (MAE) 2.14 and highest test accuracy 99.50%.

Keywords *– Brain Age Estimation, Artificial Intelligence, Deep Learning, Brain MRI Imagery, ResNet50, BAENet*

1. INTRODUCTION

A surge in instances of various non-fatal but incapacitating ailments, including neurodegenerative disorders like dementia and cognitive decline, has been seen globally with the increase in population [1]. Finding the connection between the mechanisms behind neurodegenerative diseases and brain aging processes is becoming increasingly important in order to address this problem. Techniques for determining which individuals are more vulnerable to age-related deterioration, tracking the rate of degradation, and formulating suitable treatment regimens for affected subjects must be developed. The etiology of brain illnesses is significantly influenced by age-related brain changes. The distinctions between age measured in years and age measured in the brain might indicate multiple health concerns associated with distinct life phases. In this regard, throughout the past few decades, there has been an undeniable boom in the development models for human health that are data-driven. In fact, machine learning has shown promise in a variety of modelling tasks pertaining to brain age, mostly employing brain magnetic resonance imaging (MRI) images. All of these tasks are subsumed under the general notion of brain age estimate, which uses machine learning models in conjunction with brain imaging data to predict homogenous distinct pathways in healthy brains [2]. A group of cognitively sound people for training and guided instruction—that is, a regression algorithm—are used to model the association between the patient's actual age and the extracted brain characteristics, or independent variables, in a brain age estimate framework. Patients' brain ages are hidden from the training model is then inferred by using this prediction model on independent test data. The brain's condition has been related to the divergence (positive or negative) from these usual trajectories, termed as the brain age delta, the computed brain ageless the true age, or [2]. Positive brain age delta is linked to both abnormalities in the brain and death [3] [4], but negative brain age delta is linked to a younger brain, according to a number of studies. With the use of the brain age measure, a number of neurological and psychiatric conditions have been successfully detected [5]. Apart from its application in diagnosing neurological and mental disorders, the brain age measure has been investigated in studies investigating the impact of resilience, depressive symptoms, and life satisfaction on cognitively sound brains [6].

From the review of literature, it was observed that many existing models are either CNN or CNN based approaches. However, there is need for improving CNN architecture towards leveraging performance in brain age estimation. Accordingly, we enhanced CNN model for brain age estimation. The following are our contributions to this publication. We suggested a deep learning framework that helps in automatic estimation of brain age. We also proposed a novel deep learning model and named it as Brain Age Estimation Network (BAENet). This model is based on CNN. The proposed model has increased learning capabilities in solving the problem of brain age estimation. The model has more number of layers for progressively learning the brain modality for leveraging performance. Our suggested algorithm is called

Learning based Brain Age Estimation (LbBAE). A prototype application is built for evaluation of the proposed CNN variant under the framework for estimation of brain age using brain MRI images. The remainder of the work is structured in this manner. Recent research on many approaches for estimating brain age is covered in Section 2. Section 3 provides complete details of the proposed methodology, underlying model and algorithm besides evaluation methodology. Section 4 presents results of our empirical study with the quantitative analysis. Section 5 provides discussion on the importance of the proposed methodology besides giving limitations of the study. Section 6 concludes our work and provides scope of the research for future endeavours.

2. RELATED WORK

This section reviews recent literature on brain age estimation using deep learning approaches. Dinsdale et al. [7] used brain age prediction using convolutional neural networks (CNNs) on UK Biobank data; prediction errors are correlated with clinical measures, indicating clinical significance. Peng et al. [8] used MRI data, the Simple Fully Convolutional Network (SFCN) offers a low-weight design for precise brain age prediction. Smith et al. [9] understand aging trends and illness connections is aided by analysing "brain age" derived from brain imaging data. This paper discusses problems with delta calculation and offers solutions. Beheshti et al. [10] suggested a bias-adjustment strategy that has been tested across test sets to improve brain age estimation accuracy in clinical contexts. Dular et al. [11] presented BASE, a framework that makes use of standardized datasets and criteria to assess brain age prediction algorithms.

Ganaie et al. [12] improved Twin Support Vector Regression (ITSVR), a brain age estimate method that outperforms baseline models by avoiding matrix inversions and using structural risk mitigation. Pilli et al. [13] suggested a framework for brain age estimate and classification that achieves excellent accuracy by utilizing 3D-CNN, KRR-RVFL network, and sMRI images. Constantinides et al. [14] studied on neuroimaging indicate a correlation between advanced brain age and schizophrenia. An analysis based on hereditary risk for schizophrenia revealed no differences in brain age. Tanveer et al. [15] improved the brain age prediction is aided by machine learning techniques. Review focuses on future directions, frameworks, and deep learning techniques. More et al. [16] observed that a thorough evaluation of many methods for predicting brain age showed that feature representation and machine learning algorithms had a considerable influence on reliability metrics and datasets.

Zhang et al. [17] found that systematic bias in anticipated age differences remains despite recent attempts, indicating untrustworthy phenotypes that need more research. Cali et al. [18] for privacy purposes, 'defacing,' or removing faces from MRI images, is routine. Brain age estimation accuracy is impacted by defacing; care is advised. [19] emphasized geometric deep learning (GDL) in medical imaging as it may be used with a variety of non-Euclidean data types. The special issue showcases the uses of GDL technology. Aamodt et al. [20] found a correlation between post-stroke cognitive decline and the brain age gap (BAG). A decreased BAG is eventually associated with a decreased risk of non-communicable diseases following a stroke. Zhao et al. [21] observed that in medical image analysis, deep learning—most notably CNNs—dominates and extends to non-Euclidean regions like cortical surfaces. Customized techniques improve analysis based on cortical surfaces. Wood et al. [22] stated that for clinical applications, CNNs employ structural MRI images to estimate age and identify changes from normal aging in real time. Zhang et al. [23] by integrated several machine learning methods, an age-adaptive ensemble model can precisely forecast brain age, which facilitates the formulation of treatment plans and diagnostics. Hofmann et al. [25] explored brain aging trends that are detected by combining deep learning models with Layer-wise Relevance Propagation across different MRI modalities. Leonardsen et al. [26] estimated brain age disparities by compiling large datasets, which helps with clinical prediction and reveals connections with health issues with the help of CNNs.

Engemann et al. [27] studied brain age with EEG/MEG offering more application, machine learning on brain pictures helps improve illness characterisation and measure individual aging. Gangopadhyay et al. [28] suggested MTSE U-Net achieves great accuracy in fetal brain segmentation, type prediction, and gestational age estimate. Milosevic et al. [29] used panoramic dental x-rays, deep learning automates forensic age estimate with minimal error rates for adult individuals. Taylor et al. [30] focused on a longitudinal research that examines the brain age gap (BAG) trajectory in the development of Alzheimer's disease has found that APOE 4 and sex attenuate the rapid aging seen in those with MCI. Armanious et al. [31] used deep learning for chronological age (CA) estimate and iterative data cleaning, a framework for organ-specific biological age (BA) calculation, centred on brain MRI, is presented.

Jahanshiri et al. [32] applied ensemble CNNs using MRI data, The assessment of brain age, which is crucial for the early diagnosis of neurodegenerative diseases, reaches 3.57 MAE. With a two-stage cascade network, ranking losses, and dense connections, Cheng et al.'s [33] ground-breaking 3D CNN, TSAN, surpasses current techniques in precisely determining brain age from MRI data. In an investigation into the use of machine learning to knee MRI data, Mauer et al. [34] developed a novel automated age estimation method that yielded accurate findings with potential applications in forensic medicine. The study conducted by Beheshti et al. [35] examined the impact of regression algorithms on the precision of predictions made in brain age estimation models, utilizing data from both healthy and clinical populations. Pardakhti and Sajedi [36] observed that fields of computer science and medicine have become more interested in Brain Age Estimation (BAE). Regression is accurate when using a 3D-CNN model. From the review of literature, it was observed that many existing models are either CNN or CNN based approaches. However, there is need for improving CNN architecture towards leveraging performance in brain age estimation.

3. PROPOSED FRAMEWORK

The suggested methods for estimating brain age is presented in this section. Brain MRI scans are utilized to estimate brain age using a supervised learning approach. It throws light on different aspects of the proposed methodology in the following sub sections.

3.1 Problem Definition

Provided the brain image of a patient developing a deep learning framework to calculate brain age automatically is the challenging problem considered.

3.2 Proposal Framework

As presented in suggested deep learning framework is based on figure 1 on supervised learning which has provision for data preprocessing, training, brain age estimation and validation. Our framework takes UK Biobank data set as input. The data set is subjected to pre-processing where exploratory data analysis is made to understand the data dynamics and perform required operations on data like resizing and data augmentation. Training, test, and validation sets of the data have been suitably divided.

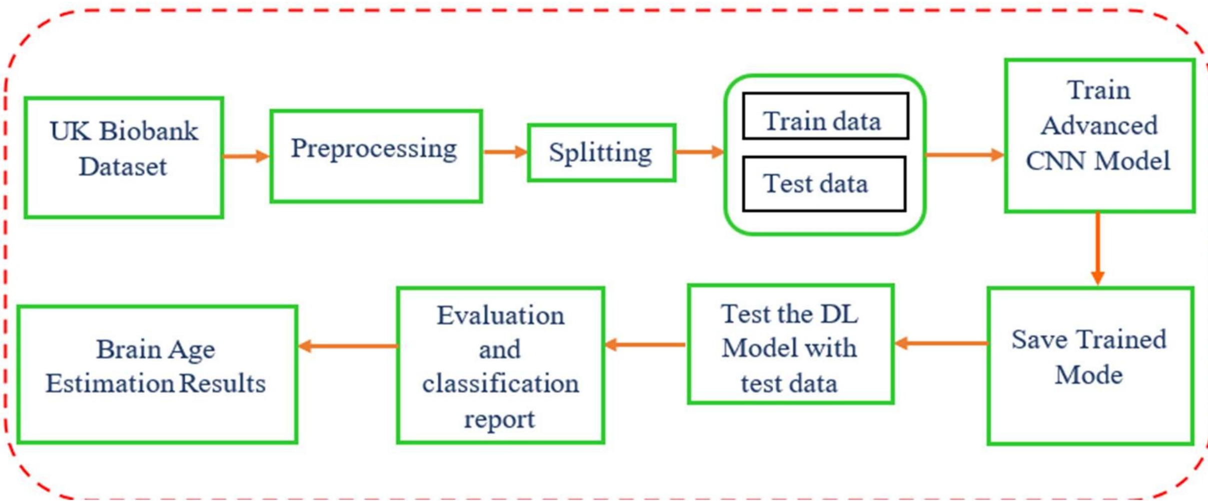


Figure 1: Overview of the proposed deep learning framework

In the process of training the proposed deep learning model known as BAENet which is a variant of CNN is used. Once the model is trained with the training set it gains required knowledge for estimation of brain age using medical image modality known as MRI. The learned model is saved for future reuse. The persistence of model is very useful retraining the model in future using transfer learning. In the process of testing the saved model is loaded in order to perform brain age estimation for every given test sample. Once the brain age estimation process is completed for every test sample the model performance is evaluated by comparing the anticipated numbers and the actual data.

3.3 Proposed Deep Learning Model

We suggested a CNN-based deep learning model. Figure 2 displays the suggested model's architecture. We refer to our model as BAENet. Using 3D T1 images, we use the BAENet architecture to estimate brain age. The design is based on the VGGNet model [46], and it makes use of a completely convolutional structure [42]. We do, however, reduce the total number of layers. Reducing parameter space to around 3 million reduces computational complexity and memory use.

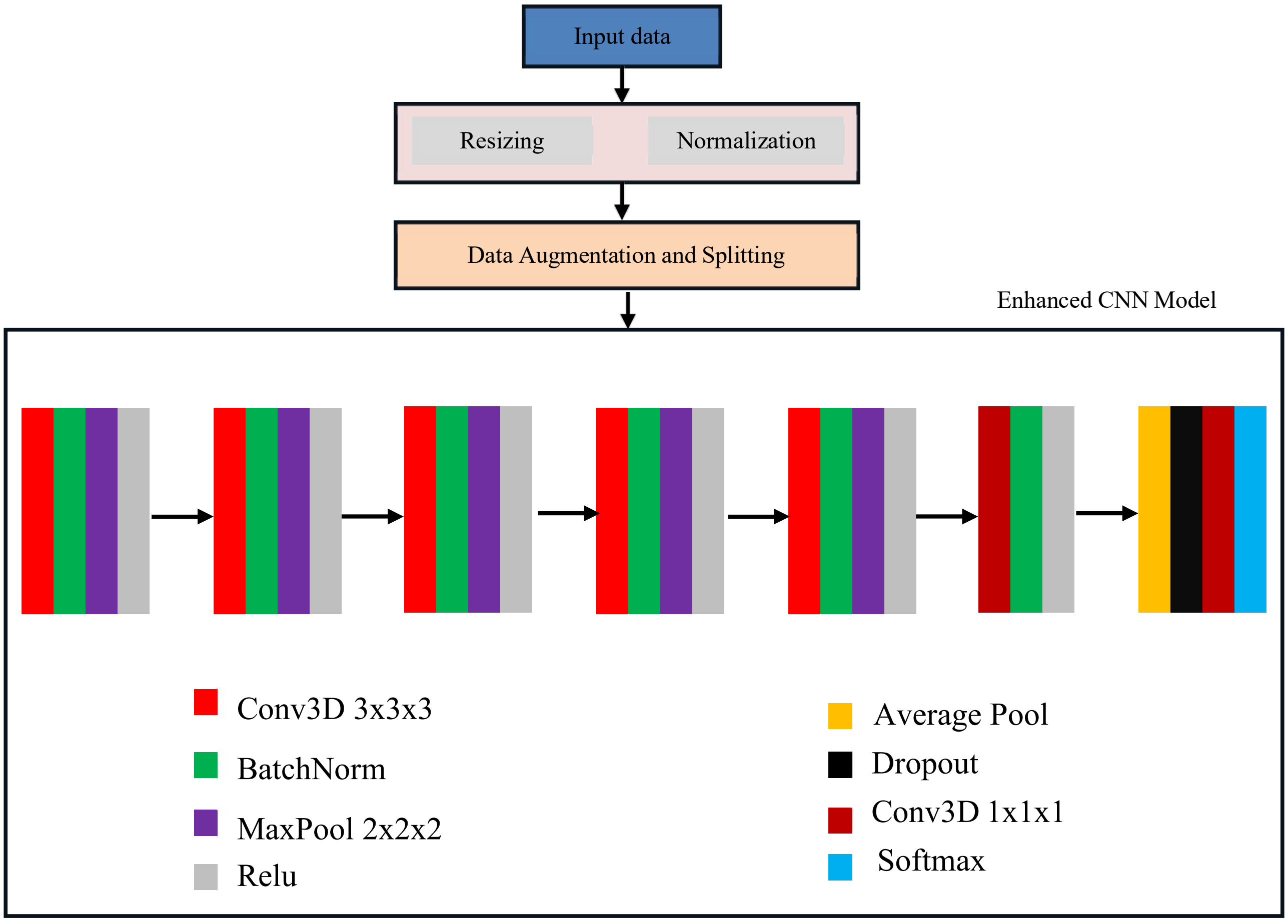


Figure 2: Architecture of the proposed BAENet model for brain age estimation

Convolutional, max pooling, batch normalization, and ReLU layers are included in each of the first five blocks [39, 41]. The input picture is processed block by block after the fifth block, after which a feature map is made and the spatial dimension is reduced to 5x6x5. Convolutional, ReLU activation, and batch normalization layers make up the block at sixth position. Seventh block: dropout layer used for training with 50% random dropout rate, fully connected layer, average pooling layer, and softmax output layer [48]. For each convolution layer, a different number of channels are employed. 40 values in the output layer indicate the expected probability that the individual's age is between 42 and 82, or between one and two years old. The weighted average of each age bin is utilized to obtain the final forecast.

as in Eq. 1.

$$pred = \sum_{c}^{40} x_c \cdot age_c \quad (1)$$

where x_c represents the expected probability for the c^{th} age bin, and age_c denotes the age interval's bin center. Three steps may be used to interpret the model's internal process: 1) Each input image's feature maps are extracted by the first five blocks. 2) The model gains an additional nonlinear layer with the inclusion of the sixth block increasing its nonlinearity even further without affecting the feature map output size. 3) The produced characteristics are mapped to the anticipated age probability distribution in the seventh block. The input picture is encoded into a feature vector in the first two stages, and the third stage makes use of a classifier. During the first phase, the majority of memory is used to preserve spatial information. We placed only one convolutional layer in each block and restricted the first layer's channel count to 32 in order to lower the total GPU memory usage. In contrast, a VGGnet typically consists of two convolutional layers within a block, with the first layer having 64 channels [46]. Fully connected (FC) layers are often the ones with the most learnable parameters in later stages in deep learning models. For example, there are around 16 million parameters in the penultimate layer of VGGnet. Reducing FC layers and ensuring less channels in the last two stages, BAENet's learnable parameter count is drastically reduced. While FC layer reduction may cause the model to learn fewer nonlinearities, in different classification approaches pertaining to neuroimaging, the number of classes is higher than in natural images. For example, there are only 40 classes for brain age prediction out of thousand classes linked to the task. In this case, the lack of FC layers and the restricted amount of parameters have no detrimental effect on testing time. We constructed a 3D version of ResNet in order to compare our BAENet with a widely used CNN architecture. 3D-ResNet's design is based on the literature, however its convolution filters are 3D instead of 2D. Both the ResNet and the BAENet use the identical training settings for the experiments and perform well in the training set.

3.4 Bias Correction

Bias correction approach illustrated in [47] is used for the delta bias correction. This type of bias correction is useful for different brain age investigations, since the prediction is usually underfit owing to issues like age distribution in non-Gaussian model and regression dilution. We fitted the desired validation set to a linear regression with the formula $x=ay+$. where yielding is the anticipated age and yielding is the chronological age. The updated anticipated age is calculated using Eq. 2.

$\hat{x} = (x - b)/a$ (2)

Using this procedure, one has to know the chronological ages at that same moment in order to determine a and b from x and y. The validation set towards corrected age delta of brain for the test samples uses previously fitted coefficients, supposing that a and b are generalizable.

3.5 Dataset Details

Brain imaging data from a large cohort of mostly healthy adults is being gathered by UK Biobank [43]. Utilizing T1 data from 14,503 individuals, we were able to conduct training on 12,949, validation on 518, and testing on 1,036. [37] provides a description of the picture preparation procedure. We used data that had previously been pre-processed on behalf of UK Biobank and that was made accessible to all researchers with access rights toKB ta. Brain extraction, bias correction, and linear registration to MNI152 standard space (unless otherwise noted) were performed on the input data before it was fed into the deep neural network model. Subjects' heads are standardized as a consequence of linear registration.

3.6 Training and Testing

For each training subject, we apply SGD optimiser [49] for the UKB dataset in order to minimize a loss function such as Kullback-Leibler divergence. The model is driven to estimate age as accurately as possible by its loss in soft categorization. Two techniques for data augmentation are used in the training phase to lessen over-fitting. Either randomly shifted inputs or inputs mirrored along the sagittal plane with a 50% probability are employed throughout each session. One may assess the model's performance in the test and validation sets using the Mean Absolute Error (MAE) [50]. Two NVIDIA P100 GPUs were used for the training of every model. To complete one training period, or training through 12,949 training subjects, the training duration was around 0.5 hours. 0.001 was the L2 weight decay coefficient. There were eight in the batch. Unless otherwise indicated, the SGD optimiser's learning rate was doubled by 0.3 every 30 epochs after being initially set at 0.01. There are 12,949 training topics in all, and there are 130 epochs. The appropriate adjustment of the epoch number ensures that the training steps are roughly the same for trials on less training data. The testing method uses the epoch that produces the best MAE. The same hyperparameters are used to train the deep learning models as we found that the models perform consistently. Within the ensemble technique, twenty models were randomly initialized and trained; five models with the same network topology Nonetheless, Randomly initialized parameters were learnt for each type of data: WM and GM, which are linearly registered; T1, which is non-linearly registered; and T1, which is linearly registered. To cut down on the total calculation time, 2,590 participants are trained in the ensemble trials. Averaging the outcomes of all 20 models is used to make the forecast.

3.8 Evaluation Methodology

Since we used learning based approach (supervised learning), metrics derived from confusion matrix, shown in Figure 3, are used for evaluation our methodology.

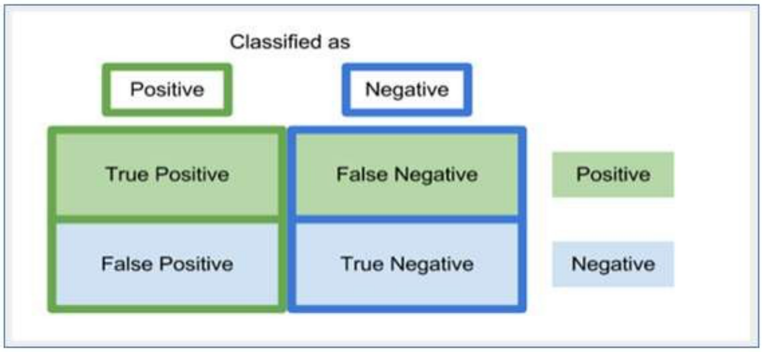


Figure 3: Confusion matrix

Based on confusion matrix, the predicted labels of our method are compared with ground truth to arrive at performance statistics. Eq. 1 to Eq. 4 express different metrics used in the performance evaluation.

$$\text{Accuracy} = \frac{TP+TN}{TP+TN+FP+FN} \quad (3)$$

The measures used for performance evaluation result in a value that lies between 0 and 1. These metrics are widely used in machine learning research.

$$\text{MAE} = \frac{1}{N}\sum_{i=1}^{N} |Pred_i - age_i| \quad (4)$$

Mean Absolute Error (MAE) is another metric used for performance evaluation as expressed in Eq. 4.

4. EXPERIMENTAL RESULTS

The results of our studies are shown in this section with respect to brain age estimation. The proposed framework and the underlying deep learning model BAENet are evaluated using UK biobank dataset which is widely used benchmark dataset. Experiments are made with data set and the observations are made in terms of accuracy and Mean Absolute Error (MAE). Figure 4 shows an excerpt from UK biobank dataset.

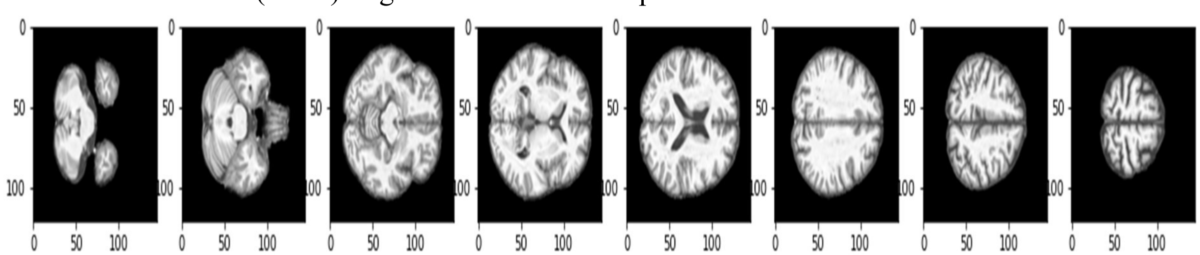


Figure 4: An excerpt from UK biobank dataset

In the experiments, the given test data is nothing but brain MRI different people. The notion of the label is used in the experiments. The soft label, distribution probability, and ground-truth are used to compute the KL-divergence loss. This allows the loss function to smoothly decline as the prediction gets better over the training period. Figure 5 shows the soft label and the prediction of the suggested brain age estimate model. The results are observed with GPU based brain age estimation.

Soft Label	Prediction

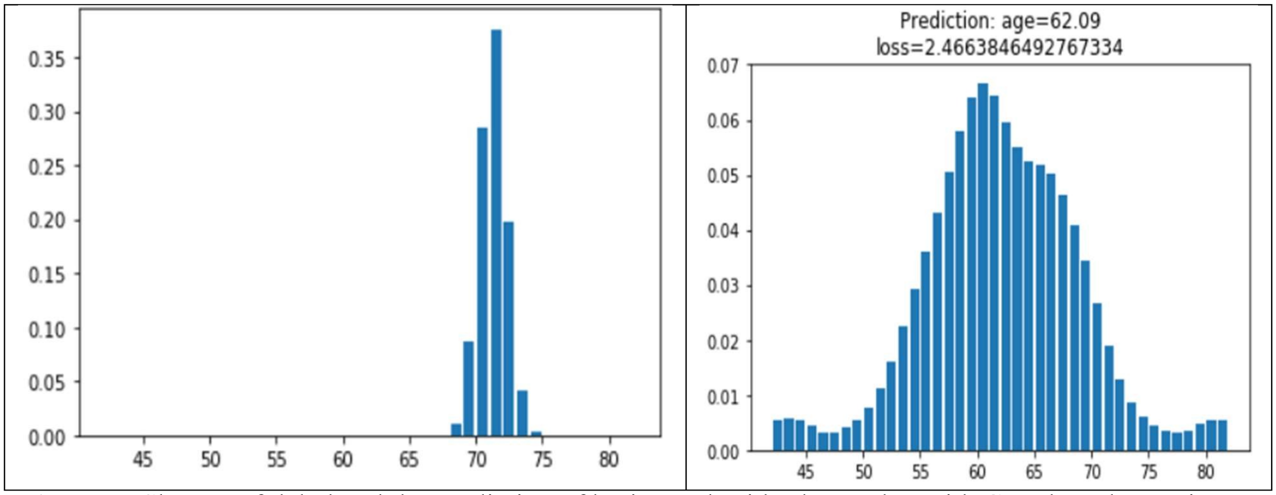


Figure 5: Shows soft label and the prediction of brain age besides loss value with GPU based experiments

Using the CPU version, the brain age is also estimated. Figure 6 displays the findings of brain age estimate using a CPU.

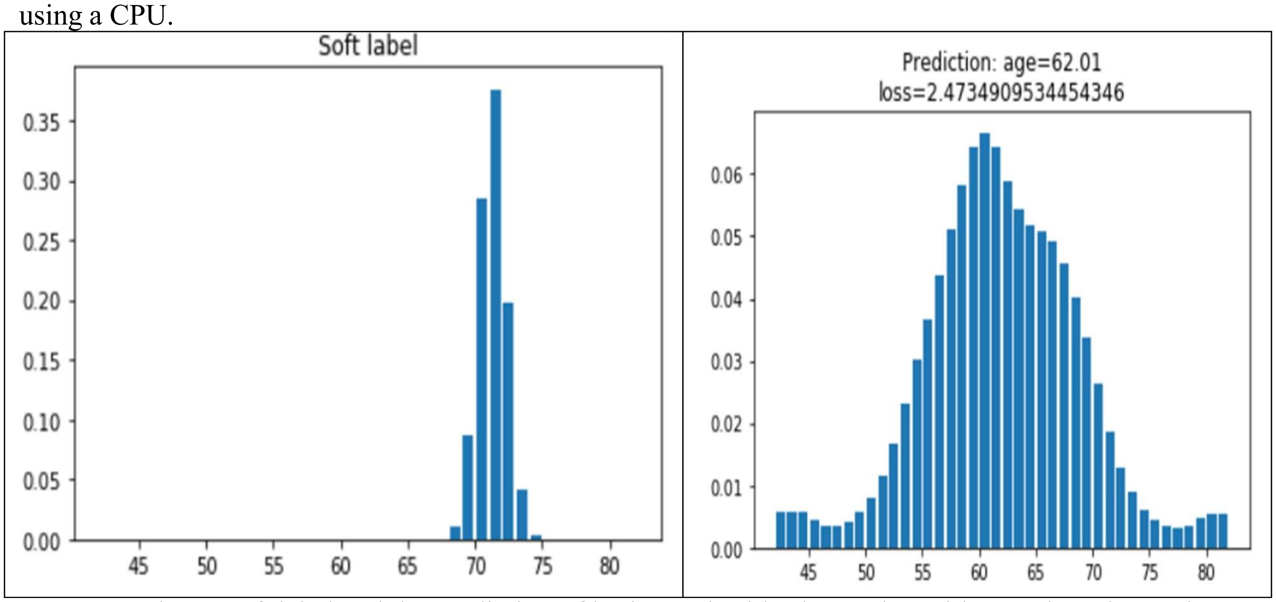


Figure 6: Shows soft label and the prediction of brain age besides loss value with CPU based experiments

The proposed deep learning model is used with two optimizers known as Adam and SGD. The model's performance is contrasted with that of the ResNet50 model using the identical optimizers. The results of deep learning models are presented in Table 1 in terms of MAE.

Age Estimation Model	**MAE (Testing) In years**	**MAE (Validation) In years**	**MAE (Training) in years**	**MAE gap (validation-training) in years**
BAENet (ADAM)	2.14	1.98	1.29	0.69
BAENet (SGD)	2.32	2.18	1.36	0.83
ResNet50 (ADAM)	2.39	2.6	1.61	0.993
ResNet50 (SGD)	2.41	2.43	1.85	0.58

Table 1: Performance of the deep learning models in terms of mean absolute error

The proposed learning model and ResNet50 are compared for their performance in brain age estimation. The mean absolute terror is provided in terms of difference in years. Figure 7 shows the performance of proposed model and also ResNet50 model with both Adam optimizer and SGD optimizer.

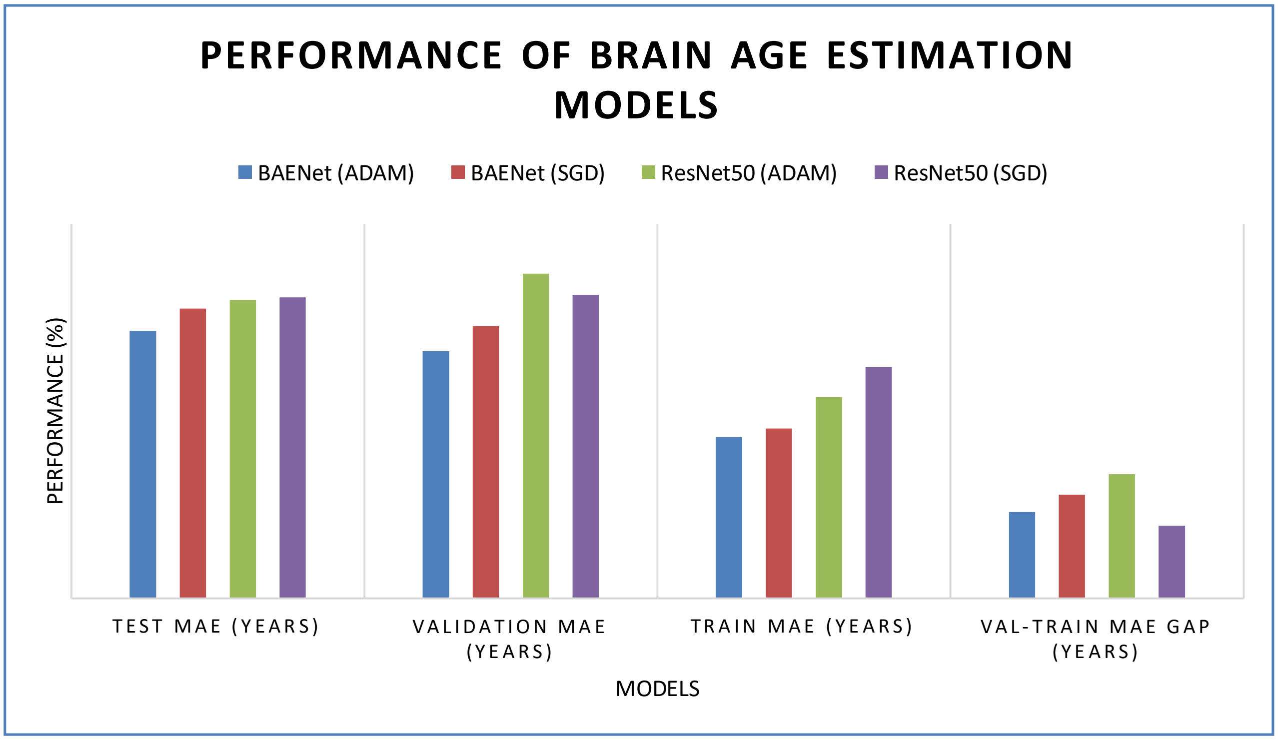


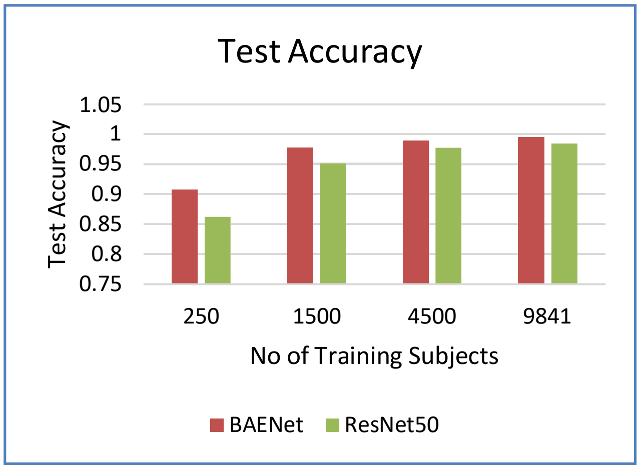
Figure 7: Performance comparison between the proposed model and ResNet50 model

How well the two deep learning models do in determining the age of a certain brain MRI sample is assessed. The difference in age between the ground truth and the forecasts is used to compare performance in terms of mean absolute error. BAENet model with Adam optimizer showed 2.14 as test MAE, 1.98 validation MAE and 1.29 train MAE. BAENet model with SGD optimizer showed 2.32 as test MAE, 2.18 validation MAE and 1.36 train MAE. ResNet50 model with Adam optimizer showed 2.139 as test MAE, 2.6 validation MAE and 1.61 train MAE. ResNet50 model with SGD optimizer showed 2.41 as test MAE, 2.43 validation MAE and 1.85 train MAE. From the results it was observed that with both Adam and SGD optimizers the proposed deep learning model BAENet performed better than ResNet50 model in terms of MAE. Table 2 shows performance accuracy-wise of deep learning models.

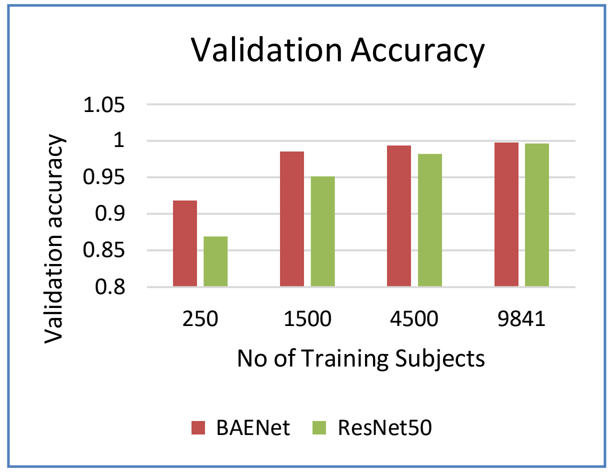
# Training Subjects	Test Accuracy (%)		Validation Accuracy (%)		Training Accuracy (%)	
	BAENet	ResNet50	BAENet	ResNet50	BAENet	ResNet50
250	0.907	0.862	0.918	0.869	0.926	0.951
1500	0.977	0.951	0.985	0.951	0.997	1
4500	0.989	0.977	0.993	0.982	1	1
9841	0.995	0.984	0.997	0.996	1	1

Table 2: Performance of deep learning models in brain age estimation

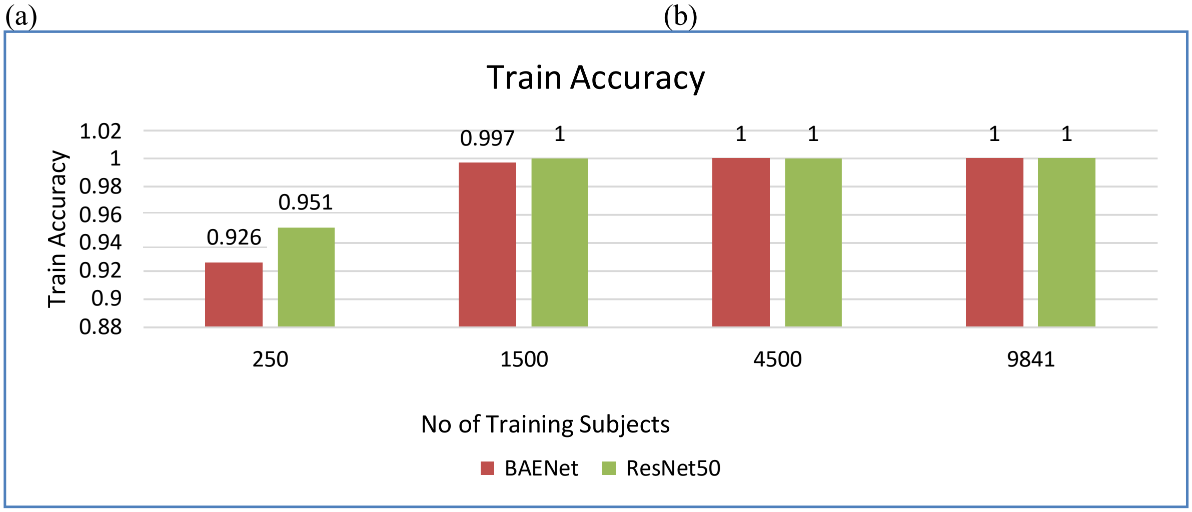
Two deep learning models' accuracy is assessed in relation to varying numbers of training subjects. Stated differently, experiments are conducted using a larger number of training samples to better understand how the models perform as they approach convergence. The test accuracy, validation accuracy, and training accuracy of deep learning models are displayed in Figure 8.



(a)



(b)



(c)

Figure 8: Performance of deep learning models in terms of test accuracy, validation accuracy and training accuracy

As soon as the quantity of training subjects is 250, the test accuracy of BAENet is 90.70% and the ResNet50 is 86.20%; the validation accuracy of BAENet is 91.80% and ResNet50 is 86.90%; the training accuracy of BAENet 92.60% and ResNet50 is 95.10%. When the quantity of trainees is 1500, the test accuracy of BAENet is 97.70% and the ResNet50 is 95.10%; the validation accuracy of BAENet is 98.50% and ResNet50 is 95.10%; the training accuracy of BAENet 99.70% and ResNet50 is 100%. When the quantity of trainees is 4500 the test accuracy of BAENet is 98.90% and the ResNet50 is 97.70%; the validation accuracy of BAENet is 99.30% and ResNet50 is 98.20%; the training accuracy of BAENet 100% and ResNet50 is 100%. As soon as the quantity of training participants reaches 9841 the test accuracy of BAENet is 99.50% and the ResNet50 is 98.40%; the validation accuracy of BAENet is 99.70% and ResNet50 is 99.60%; the training accuracy of BAENet 100% and ResNet50 is 100%.

5. DISCUSSION

Brain age estimation is an important research to know the patterns and understand whether a person has correct aging pattern or not. In this research, from the literature review, we understood that most CNN is the deep learning model that is used to analyze medical picture data. Another important observation is that the CNN model has capability to extract rich features from given medical image. Provided brain MRI as modality for this research CNN model is capable of learning features from brain MRI images. This is the rationale behind using CNN based models in our research. In fact, we proposed a novel architecture based on CNN. Our model is known as BAENet. The proposed deep learning architecture is evaluated with the benchmark dataset known as UK biomark dataset which is widely used in the brain related research. Utilizing both Adam and SGD optimizers, the suggested deep learning model is assessed. Another deep learning model known as ResNet50 is used for comparing the experimental results. From our iempirical study we understood that with supervised learning, one may estimate the age of the brain.The deep learning model that is being suggested is ssessed using accuracy and mean absolute error as metrics. The BAENet proposed in this paper can be used as part of clinical decision support system used by healthcare units.

5.1 Limitations

The proposed methodology followed in this paper has certain limitations. We made experiments with only one medical image modality MRI. Experiments are not made with other modalities like CT scan. Another important shortcoming of the paper is that proposed model is based on CNN and it needs to be investigated further in order to evaluate with real time samples collected from healthcare units. The proposed deep learning model is evaluated with only one dataset known as UK biomark data set. There may be threats to validity of the findings in the empirical study unless the model is evaluated with different medical imaging modalities and different benchmarking data sets.

6. CONCLUSION AND FUTURE WORK

We proposed a deep learning framework that helps in automatic estimation of brain age. Our framework takes UK Biobank data set as input. The data set is subjected to pre-processing where exploratory data analysis is made to understand the data dynamics and perform required operations on data like resizing and data augmentation. In the process of training the proposed deep learning model known as BAENet which is a variant of CNN is used. Once the model is trained with the training set it gains required knowledge for estimation of brain age using medical image modality known as MRI. In the process of testing the saved model is loaded in order to perform brain age estimation for every given test sample. Once the brain age estimation process is completed for every test sample the model performance is evaluated by comparing the ground truth and the predicted values. We also proposed a novel deep learning model and named it as Brain Age Estimation Network (BAENet). This model is based on CNN. The proposed model Has increased learning capabilities in solving the problem of brain age estimation. The model has more number of layers for progressively learning the brain modality for leveraging performance. We introduced the Learning based Brain Age Estimation (LbBAE) technique. Our empirical investigation uses the UK Biobank benchmark data set. The suggested model surpassed ResNet50 with the maximum test accuracy of 99.50% and the lowest MAE of 2.14, according to the experimental findings. In order to increase the accuracy of brain age estimation, we want to investigate various pre-trained deep learning models using transfer learning-based improvements in the future.

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