

## Age Prognostication Using Machine Learning From Brain PET, CT and MRI Images

Shubhangi D C<sup>1</sup>, Baswaraj Gadgay<sup>2</sup>, Khaleda Begum<sup>3</sup>

<sup>1</sup>Department of Computer Science, Visvesvaraya Technological University CPGS Kalaburgi, Karnataka, India

<sup>2</sup>Department of Electronics and Communication, Visvesvaraya Technological University CPGS Kalaburgi, Karnataka, India

<sup>3</sup>Department of Computer Science, Visvesvaraya Technological University CPGS Kalaburgi, Karnataka, India

ARTICLE INFO	ABSTRACT
<b>Published Online:</b> <b>06 June 2024</b>	Software provides a high-level introduction to methods of brain age prediction & their potential therapeutic applications. Brain-aging research employs regression machine learning model to predict neuroanatomical changes as people become older. This model is subsequently employed to estimate cranial ages of newly-observed participants. A person's "brain-age gap" is difference between their expected brain age & their actual age. This value may be a sign of general brain health and is hypothesized to represent neuro-anatomical abnormalities. It may support differential diagnosis, prognosis, and therapy decisions as well as early detection of brain-based illnesses. These applications may result in earlier and more focused therapies for illnesses associated with ageing. Our experimental findings show that regression algorithms have an impact on the brain age frameworks' prediction accuracy, suggesting that more sophisticated machine learning techniques may improve brain age predictions in clinical contexts. Additionally, the experiment is being run on several scan pictures, including CT, MRI, and PET. Based on estimating brain age, disease type and stages are detected.
Corresponding Author: <b>Shubhangi D C</b>	
<b>KEYWORDS:</b> brain age, CT, MRI, PET, regression, neuro-anatomical	

### I. INTRODUCTION

Ageing and the health problems it is associated with pose a significant challenge to people and society everywhere. Growing attempts are being made to identify age-related disorders early with the ultimate goal of avoiding or slowing their progression in order to meet this challenge. Brain age prediction is a method that leverages on the well-established correlation between age and neuro-anatomy across the lifetime [1] to quantify impacts of ageing upon brain. All utilise of structural neuroimaging data and machine learning techniques. Data patterns are discovered using machine learning models, which are subsequently used to predict the outcomes of fresh data. Making inferences at the individual level as opposed to the group level with these methodologies above standard statistics increases the possibility of medical transformation [2]. In order to forecast a person's brain's age, researchers often construct machine learning regression model utilizing structural MRI information obtained from healthy controls.

### II. RELATED WORK

This study compiles findings from the previous decade's [1] worth of research which has utilized BrainAGE approach to assess how factors including communication, environment, genetics, life load, illnesses, & time affect neuroanatomical aging throughout course of individual's lifetime. The 'brain-predicted age' presented here is one such biomarker, and it was developed utilizing structural neuroimaging studies. In order to assess associations between age-related functional parameters & mortality, Lothian Birth Cohort of 1936 (N=669) were utilized for testing machine-learning model that had been built using neuroimaging data by an enormous healthy reference population (N=2001). The employment of machine-learning algorithms & brain scans allowed for the estimation of an individual's "brain age" [3]. The notion which pathologic atrophy observed in Alzheimer's disease (AD) can be considered an expedited aging process, leading to increased degeneration of brain, is substantiated by evidence indicating as early detection of deviations in brain anatomy, like those seen in AD, has a chance to enhance clinical outcomes by

enabling timely intervention. A model of normal brain aging is required before accelerated atrophy of the brain may be recognized.

In order to identify and monitor neurodegenerative disorders, neuroimaging-driven brain age estimate has provided a strong biomarker.[5] Using T1-weighted MRI scans & models of gray & white matter, authors here calculate brain ages of AD & PD patients to compare them. Epilepsy is hallmark of psychosis as well as beyond, and now we can use neuroimaging to estimate how old someone's brain is.[6] In order to identify and monitor neurodegenerative disorders, neuroimaging-driven brain age estimate has provided a strong biomarker. This model is subsequently applied on unseen participants to estimate their mental age. [13] 'Brain-age gap' refers to the disparity amongst individual's estimated mental age and their actual age. Age prediction utilizing brain morphological features[14] may aid in discovery of aberrant aging process due to fact that brain structural morphology changes throughout course of aging trajectory.

### III. PROPOSED SYSTEM

To reliably estimate brain age values for clinical applications, robust prediction model inside brain age estimation framework is required. Gaussian process regression & SVM are two of most utilized regression techniques. Taking into account regression technique for estimating brain age.

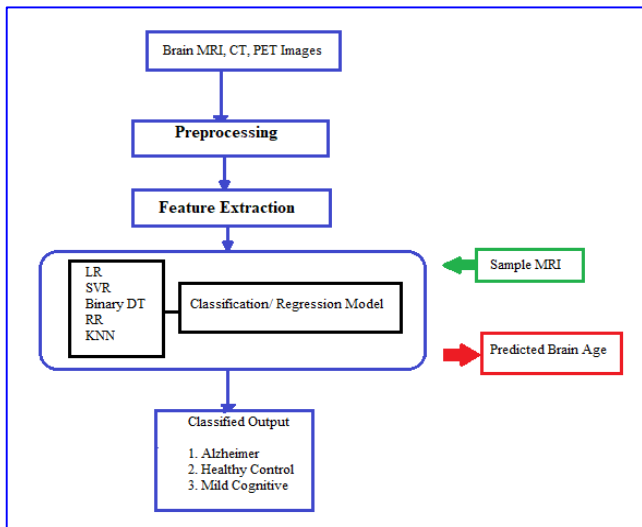


Figure 1: Proposed Model

### IV. METHODOLOGY

PET, MRI, or CT scans are used as input in suggested approach. Classification/Regression models like KNN, LR, SVR, & Binary DT model are all put to use with impressive results by system. Also, these classifiers can determine if a person has Alzheimer's, healthy cognition, or mild cognitive impairment & anticipate their brain age. Our goal was to compare precision of several regression methods for determining a person's mental age. The following is an explanation of several regression methods used in this research to determine an individual's brain age:

**Linear Regression:** Linear Regression is a method for modeling the connection between a dependent variable that is continuous and a set of categorical explanatory factors. Parameters of the linear predictor function used to model this association are estimated from data. Although least-squares method is often used to fit linear regression models, alternative methods of fitting are possible.

#### Support Vector Regression:

By finding hyperplane and reducing variance among predicted values & correct labels, SVR may reduce error. Besides its superior performance, SVR is advantageous because of its adaptability toward geometry, transmission, data-generalization, & the inclusion of extra kernel features. This new feature improves model's predictive ability by taking feature quality into account.

#### Algorithm of SVM:

Input:  $S, \lambda, T, k$   
 Initialize : Choose  $w_1$  s.t.  $\|w_1\| \leq 1/\sqrt{\lambda}$   
 For  $t = 1, 2, 3, \dots, T$   
     Choose  $A_t \subseteq S$ , where  $|A_t| = k$   
     Set  $A_t^+ = \{(x, y) \mid A_t: y(w_t, x) < 1\}$   
     Set  $n_t = 1/\lambda t$   
     Set  $w_{t+1/2} = (1 - n_t \lambda) w_t + n_t / k (x, y) A_t^+ y^x$   
     Set  $w_{t+1} = \min\{1, 1/\sqrt{\lambda}\} \|w_{t+1/2}\| w_{t+1/2}$   
 Output :  $w_{T+1}$

As its useful properties and straightforward calculation in a high-dimensional feature space, we regression (SVR) technique to serve as the basis of our framework for estimating the brain's age. This is a representation of linear regression function  $f(x)$ .

$$f(x) = \omega \cdot \varphi(x) + b \quad (1)$$

where  $x$  is input space &  $\varphi$  signifies kernel function. Furthermore, slope offset is represented by  $w$ , while regression line offset is denoted by  $b$ .

We determined age estimator's precision utilizing MAE & RMSE as follows:

$$MAE = [1/n * \sum_i |g'_i - g_i|] \quad (2)$$

$$RMSE = [1/n * \sum_i |(g'_i - g_i)^2|]^{1/2} \quad (3)$$

here  $n$  is number of subjects in testing sample, &  $g'_i$  &  $g_i$  signify estimated age & chronological age, correspondingly.

**Binary Decision Tree:** BDT is a kind of supervised machine learning that uses a succession of binary judgments to evaluate characteristics. The following two outcomes may occur after every decision is made: whether a different decision or forecast. In regression tree, independent variables are used to fit a regression model to the dependent variable. Information is then partitioned many times for every variable that is independent. For every instance, we calculate SSE by squaring the difference among anticipated as well as actual values. Split point is determined by comparing SSE across all of variables

and selecting one with lowest value. Recursive procedure is repeated until expected output value can be calculated.

*GenDecTree(Sample S, Features F)*

**Steps:**

1. **If** *stopping\_condition(S,F)=true* **then**
  - a. *Leaf = createNode()*
  - b. *leafLabel = classify(s)*
  - c. **return** *leaf*
2. *root = createNode()*
3. *root.test\_condition = findBestSplit(S,F)*
4.  $V = \{v \mid v \text{ a possible outcome of } \text{root.test\_condition}\}$
5. **For each** value  $v \in V$ :
  - a.  $S_v = \{s \mid \text{root.test\_condition}(s) = v \text{ and } s \in S\}$ ;
  - b. *Child = TreeGrowth (S<sub>v</sub>,F)*;
  - c. *Add child as descent of root and label the edge {root → child} as*
6. **return** *root*

**Ridge Regression:** When analyzing data with multi-collinearity, ridge regression is useful model tuning technique. L2 regularization is used in this approach. In presence of multi-collinearity, variances tend to be large while least-squares methods tend to be objective. Therefore, there is a significant discrepancy between expected and observed values. Ridge regression incorporates little bias factor into the variables to correct for this. Regression of age on brain traits typically produces a biased model, with younger people's ages being overestimated and older people's ages being underestimated. There is a negative ADC between  $y$  and  $x$ , indicated by  $\text{corr}(y, x)$ . In scientific literature, ADC was made equal to zero by doing second step of analysis to rectify first stage's regression predictions. Thus, following two-step process may be used to forecast a person's brain age:

- (a) Brain Age Prediction. Create model  $f$  of age prediction where  $y \approx f(X)$ . The unfavorable residuals are indicated by  $\delta = f(X) - y$  ---(7) portrays uncorrected brain age delta.
- (b) Correcting Brain Age Delta. In order to eliminate ADC, many writers have suggested rectification strategies. There is mathematical parity between several of these methods. They reduce to two methods, one producing a corrected residual of 1 and the other of 2. Two sections that follow provide in-depth discussions of these two methods.

**Gaussian Processes for Regression:** Non-parametric regression describes this method. Instead of computing likelihood distribution of a single function's parameters, it does it across all acceptable functions which satisfy data. Due to extensive availability of different kernel functions for Gaussian processes, it may be utilized for wide range of datasets.

**k-Nearest Neighbors (KNN):** The original purpose of this technique was to do classification, however it was subsequently modified to perform regression as well. This method selects the 'k' closest samples by dataset to target object. Closest neighbors of item are determined using Euclidean distance using method. The final result is calculated by taking the mean of outputs

of closest 'k' neighbors. Accuracy of original method may be improved with tweaks like Weighted Meanrule.

Let  $S = \{p_1, \dots, p_n\}$  be collection of patient readings used for training of the type  $p_i = (x_i, c_i)$ , wherein  $x_i$  is d-dimensional feature vector of point  $p_i$ , &  $c_i$  is class to which  $p_i$  belongs. Let  $k$  be required number of closest neighbors.

For every  $p' = (x', c')$

- Compute the distance  $d(x', x_i)$  between  $p'$  and all  $p_i$  belonging to  $S$
- Sort all points  $p_i$  according to the key  $d(x', x_i)$
- Select the first  $k$  points from the sorted list, those are the  $k$  closest training samples to  $p'$
- Assign a class to  $p'$  based on majority vote:  $c' = \text{argmax}_y \sum (x_i, c_i)$  belonging to  $S, I(y=c_i)$
- End

**Classification model**

Most metrics are calculated using TP, FP, TN, & FN data. The suggested modeling accurately identifies number of examples (denoted by TP) which are members of a class. The false positive rate (FP) is the amount of examples that are incorrectly assigned to a class when they really belong to another class. There are TN instances, which are those that were correctly identified as not associated with a class, and FN instances, which were incorrectly identified as not having to class. Eq. (1) may be used to determine a model's (the BAE system's) accuracy.

$$\text{Accuracy} : (\text{TP} + \text{TN}) / (\text{TP} + \text{TN} + \text{FP} + \text{FN}) \dots \dots (1)$$

Calculated using Eq. (2), sensitivity indicates percentage of true positives (TPs) which have been discovered. It's also known as TP rate, recall, or probability of detection.

$$\text{Recall} : \text{TP} / \text{TP} + \text{FN} \dots \dots \dots (2)$$

Calculated using Eq. (3), particularity, also known as TN rate, precision, is percentage of false negatives which are accurately recognized. The F-measure is derived from the proportion of correct answers using Eq. (4)

$$\text{Precision} : \text{TP} / \text{TP} + \text{FP} \dots (3)$$

$$\text{F-measure} : 2 * \text{precision} * \text{recall} / (\text{precision} + \text{recall}) \dots (4)$$

In Fig. 2, we see an example confusion matrix for MAE with 9 classes and classification algorithm. 2 samples in this table, whose actual ages are in their 6 years, were incorrectly estimated to be in their eighth. Values in diagonal columns are accurate, whereas figures in other cells reflect inaccuracy of BAE system.

**Regression model:** Some statistically based techniques for dealing with age prediction problem are presented in sequel. These metrics are often used when a regression-based modeling methodology is being utilized. Using Eq. (5), we can determine

## “Age Prognostication Using Machine Learning From Brain PET, CT and MRI Images”

the degree of correlation among actual & anticipated ages, while applying Eq. (6), we can get the total variance.

$$r = \text{Correlation (Pearson } r) \dots (5)$$

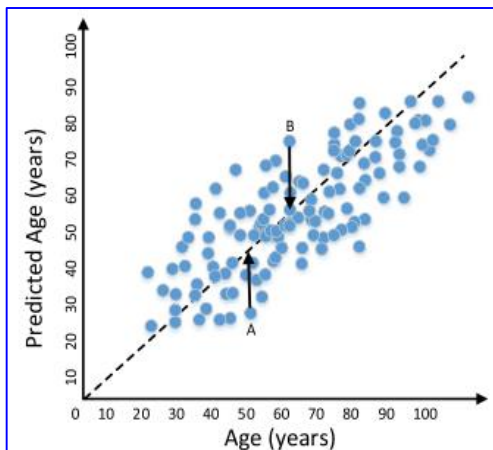
$$R^2 = \text{Total variance} \dots (6)$$

Using Eq. (7), we find that the approach has MAE for estimating subject's age of 4.0 years. RMSE, which may be calculated using Eq. (8), is another metric utilized to assess efficacy of BAE systems.

$$\text{MAE} = \sum_{i=1}^n (y_i - x_i) / n \dots (7)$$

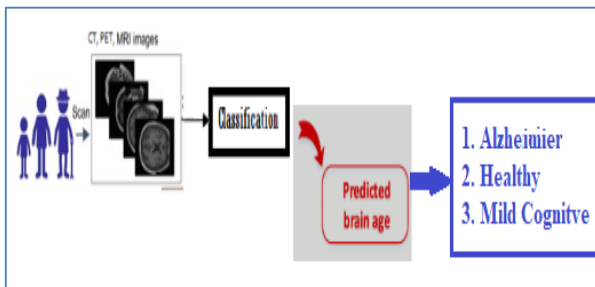
$$\text{RMSE} = \frac{\sqrt{\sum_{i=1}^n (y_i - x_i)^2}}{n} \dots (8)$$

In Figure 2, we see an example of a graph generated using a regression technique for MAE. Examples A & B in this discussion show situations in which psyche's age is younger or older than body's, respectively. If MRIs in sample represent a range of healthy patients, then the BAE error may be seen as departure from a straight line.



**Figure 2: Relationship amongst chronological age & brain in regression model**

### V. SYSTEM ARCHITECTURE



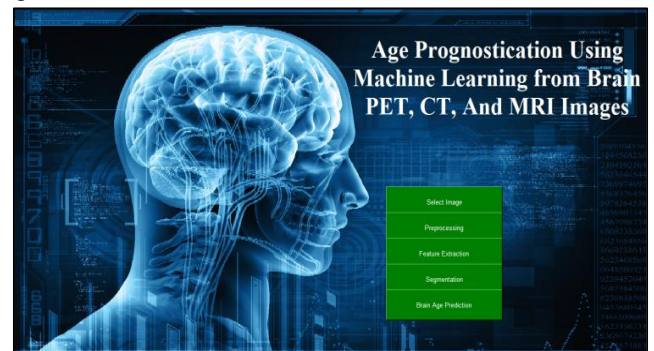
**Figure 3: System Architecture**

The above architecture consists of Input image, prediction Model, classification and prediction. The system accepts the scanned CT, PET, and MRI images. These scanned images applied to prediction model. Model predicts the brain age as per

features and further using machine learning classifiers such as SVM classifies the brain into healthy or Alzheimer.

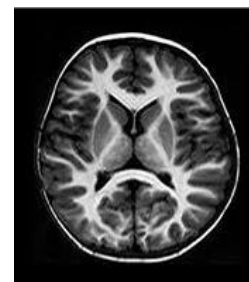
### VI. RESULTS AND DISCUSSIONS

R2 score is utilized for evaluating efficacy of linear regression model. In previous paper, Support Vector Regression algorithm R2 = 0.88, and Decision Tree algorithm R2 = 0.76. In this system, Support Vector Regression algorithm R2 = 0.90, and Decision Tree algorithm R2 = 0.78 As per previous study, implications for downstream group comparisons imply care must be given while selecting regression model to use in clinical contexts. So, in our system we are experimenting not only on MRI images but also predicting the brain age using PET, CT and MRI images based on machine learning algorithms such as SVM, DT, RF, LR.



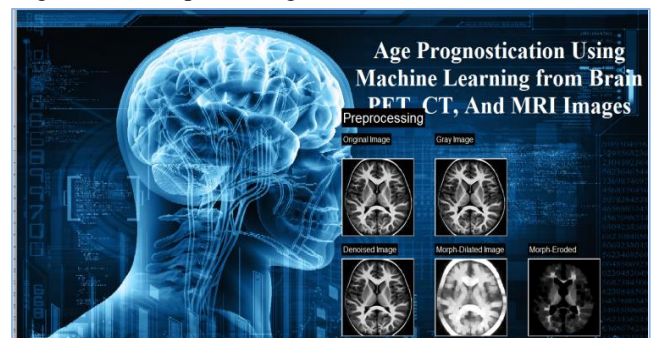
**Figure 4: Menu**

In Figure 4, we see the menu of the model which shows the different inputs to be selected as select image, preprocessing, feature extraction, segmentation and brain age prediction, to get the result.



**Figure 5: Read Image**

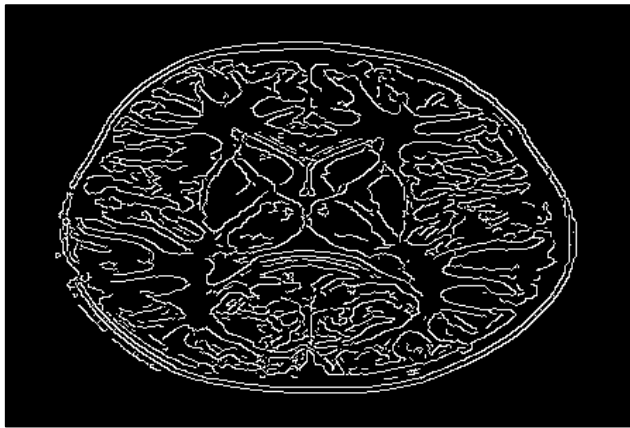
In Figure 5, we see the read image that reads out and scan the image for further processing.



**Figure 6: Preprocessing**

## “Age Prognostication Using Machine Learning From Brain PET, CT and MRI Images”

In Figure 6, we see the different preprocessing images which shows the different filters of the image’s quality so that it can analyze it more effectively.



**Figure 7: Feature Extraction**

In Figure 7, we see the feature extraction which is defining the behavior of an image, which shows the efficiency in classification.



**Figure 8 : Threshold Image**

In Figure 8, we see the partitioning image into a foreground and background. This image analysis technique is a type of image segmentation that isolates objects by converting grayscale images into binary images.

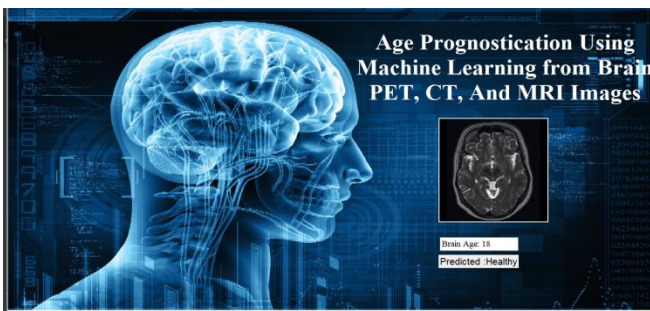


Figure 9: Prediction In Figure 9, It shows the predicted Brain age and the category of brain is healthy.

**Table I: Model Accuracy**

Model	Accuracy	R2-Score
DT	83%	0.68
RF	88%	0.48
SVM	90%	0.90

In Table I of model accuracy, it is determining which model is best at identifying relationships and patterns between variables in a dataset based on the input, or training data. So therefore model SVM is determining the model accuracy.

### VII. CONCLUSION

From this concluded that the set out to thoroughly assess different regression model for calculating brain ageing, not just in healthy persons even into medical populations. On a dataset made up of mentally healthy people like training set, we evaluated various regression models. Then, using independent test sets made up of MCI participants, AD patients, and mentally healthy persons, we quantified each regression model. Our thorough analysis indicates that the choice of regression model in clinical settings should be cautious since it may affect subsequent comparisons between groups. In this system, used various regression models such as LR, SVR, KNN, DT. Based on this it predicts the age and classifies in terms of Alzheimer, Healthy and Mild Cognitive. Future comparisons between our suggested brain age estimation using ML and numerologically based age calculation will be made.

### REFERENCES

1. K. Franke and C. Gaser, “Ten years of brainage as a neuroimaging biomarker of brain aging: What insights have we gained?,” *Front. Neurol.*, vol. 10, p. 789, 2019.
2. J. H. Cole et al., “Brain age predicts mortality,” *Mol. Psychiatry*, vol. 23, no. 5, pp. 1385–1392, 2018.
3. I. Beheshti, S. Nugent, O. Potvin, and S. Duchesne, “Disappearing metabolic youthfulness in the cognitively impaired female brain,” *Neurobiol. Aging*, vol. 101, pp. 224–229, 2021.
4. K. Franke, G. Ziegler, S. Klöppel, C. Gaser, and A. D. N. Initiative, “Estimating the age of healthy subjects from T1-weighted MRI scans using kernel methods: Exploring the influence of various parameters,” *Neuroimage*, vol. 50, no. 3, pp. 883–892, 2010.
5. I. Beheshti, S. Mishra, D. Sone, P. Khanna, and H. Matsuda, “T1-weighted MRI-driven brain age estimation in Alzheimer’s disease and Parkinson’s disease,” *Aging Dis.*, vol. 11, no. 3, pp. 618–628, 2020.
6. D. Sone et al., “Neuroimaging-based brain-age prediction in diverse forms of epilepsy: A signature of psychosis and beyond,” *Mol. Psychiatry*, vol. 26, pp. 825–834 Mar. 2021.
7. I. Nenadić, M. Dietzek, K. Langbein, H. Sauer, and C. Gaser, “Brainage score indicates accelerated brain aging in schizophrenia, but not bipolar disorder,” *Psychiatry Res.: Neuroimaging*, vol. 266, pp. 86–89, 2017.
8. I. Beheshti, P. Gravel, O. Potvin, L. Dieumegarde, and S. Duchesne, “A novel patch-based procedure for

- estimating brain age across adulthood,” *NeuroImage*, vol. 197, pp. 618–624, 2019.
9. A. Cherubini, M. E. Caligiuri, P. Péran, U. Sabatini, C. Cosentino, and F. Amato, “Importance of multimodal MRI in characterizing brain tissue and its potential application for individual age prediction,” *IEEE J. Biomed. Health Informat.*, vol. 20, no. 5, pp. 1232–1239, Sep. 2016.
  10. J. H. Cole, “Multimodality neuroimaging brain-age in U.K. biobank: Relationship to biomedical, lifestyle, and cognitive factors,” *Neurobiol. Aging*, vol. 92, pp. 34–42, 2020.
  11. J. H. Cole, R. Leech, D. J. Sharp, and A. D. N. Initiative, “Prediction of brain age suggests accelerated atrophy after traumatic brain injury,” *Ann. Neurol.*, vol. 77, no. 4, pp. 571–581, 2015.
  12. J. H. Cole et al., “Increased brain-predicted aging in treated HIV disease,” *Neurol.*, vol. 88, no. 14, pp. 1349–1357, 2017.
  13. Lea Baeckera, \*, Rafael Garcia-Diasa , Sandra Vieiraa , Cristina Scarpazzaa,b , Andrea Mechelli “Machine learning for brain age prediction: Introduction to methods and clinical applications”, 2021
  14. Juhyuk Han,Seo Yeong Kim, Junhyeok Lee,Brain Age Prediction: A Comparison between Machine Learning Models Using Brain Morphometric Data, 2022