# A Survey on Brain Age Prediction Models

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*Abstract* - **Brain age is simply the age predicted from MRI images. As age of a person increases there will be some changes in brain structure which will be different for male and female. Brain Aging has a deeper connection with white matter and gray matter concentration. Hence if there is a diversification in the concentration of white matter and gray matter it will affect aging of brain. Brain Age has been proven as a biomarker for finding neurodegenerative diseases. In this study, here summarize various prediction methods which is used for brain age estimation in last 11 years. The study will include dilemmas in the study and future possibilities of brain age proposed by existing models.**

*keywords* - **Brain age, survey, Brain age prediction models.**

## I.INTRODUCTION

The Brain age concept is now having popularity in real world. Human Brain will get aged as the chronological age of human beings increased. During aging process structure and functionalities of brain will not remain the same as before. As age increases the frontal cortex will shrink. The brain activities related to memory task will gradually be ineffective as the brain ages. The episodic and semantic memory functions will be mostly affected with brain aging process. Also brain aging has deeper connections with the concentration of grey matter and white matter. Theoretically brain age is the age predicted from MRI scans of Healthy subjects. When compared with chronological age which is the calendar age, brain age could be slightly different. That difference between calendar age and chronological age is called brain age gap or brain age difference. Brain Age can be accurately estimated from different models. The size of data samples and their age range will determine how accurate is the prediction.

Brain age is a broadly used biomarker for evaluating and estimating various neuro-degenerative diseases. Hence brain age can be used as a key to various studies related to neurology. Neuro-degenerative diseases affect our body activities and this led to severe conditions in affected individuals. The individuals affected with Alzheimer’s Disease (AD) and Parkinson’s Disease (PD) may unable to perform body activities such as breathing, talking, balance and movements. Hence AD and PD and other neurodegenerative diseases which needs more attention can be detected using brain age predicted from MRI images.

The research summarizes that brain age can be accurately predicted by different prediction models. Brain Age Prediction based on various model is discussed in Section II. Comparative study of different brain age prediction model and datasets used is tabularized in Section III and IV. The problems identified from the models is summarized in Section V. Brain age is proved as a criterion for predicting and classifying several neurodegenerative diseases. The future possibilities of brain age predicted from MRI images is discussed in Section VI.

## II.RESEARCH ON VARIOUS BRAIN AGE PREDICTION MODELS

### A.Based on Structural Connectivity using Artificial Intelligence

Brain Aging has a deeper connection with white matter and gray matter concentration. Hence if there is a diversification in the concentration of white matter and gray matter it will affect aging of brain. Diffusion Tensor Imaging [1] is used to explore the diversity in topology of white matter in brain and their structural connectivity in people who are old. The topological diversity occurs during the aging of healthy people and it can be used as a biomarker to predict the brain age. To detect the topological diversity in white matter of brain DTI Tractography can be used to build white matter networks. Principle Component Analysis with back propagation artificial neural network(BPNN) can be used to estimate brain age.

### B. Based on CNN and Deep Neural Networks.

CNN predicted age [2] can be effectively used to estimate brain age of a person with the help of structural neuroimaging data. A 3D CNN [3] which is light weighted will perform better than the deep CNN in brain age prediction. A deep learning [4] model with in taking MRI as input along with brain age gap or brain age difference can be used to analyze the risk of dementia. A 3D CNN with simpler model [5] is most commonly used in models which are linear and nonlinear.

### C. Based on Sparse Representation Method

A voxel selection method [6] based on sparse can be used to find out various regions of brain. Age prediction will be based on grey matter concentration map. Due to aging voxels tends to change, sparse representation method can be used to actively select the voxels.

### D.Based on Cortical Structure

Brain age prediction is possible from analyzing cortical structure [7] using large volumes of structural MRI. Thickness, gyrification and dimensionality are the three measures of cortical morphology. To find out the which cortical structure will predict brain age of a single person accurately, parcellation techniques are identified.

E. Based on High Resolution Pattern recognition

High dimensional pattern recognition [8] will permit evaluating brain age automatically. More sophisticated aging pattern is transfigured into brain age index potently. The sign of brain age index will signify that whether brain is having negative sign or positive sign. To build healthy aging pattern of brain RVR (Relevance Vector Regression), a machine learning model is used.

F. Based on Hidden Markov Model

Hidden Markov Model [9] is a mathematical approach for simulating MRI-based structure of brain. Wavelet coefficient is used to extract valuable features from brain MRI. Vector quantization procedure is used to code the wavelet coefficient. Brain age of individuals can be discovered by some brain component features which are intra-cortical tissues, CSF and grey matter.

G. Based on Multimodal Imaging

Multimodal [10] data improves brain age prediction by utilizing cortical anatomy and functional connectivity. Stacked multimodal approach is optimum for prediction of brain age. The individuals with OCI (Objective Cognitive Impairment) shows increased aging of brain while using multimodal approach. Correlation was analyzed [11] between chronological age and predicted brain age to probe the accuracy of brain age prediction.

H.Estimation from T1 weighted MRI using Machine Learning.

Brain Age gap obtained after evaluating brain age can be used as a biomarker to find out the contrast between Alzheimer's disease [AD]and Parkinson disease [PD] subjects. T1 weighted MRI scans and high level machine learning models can be used to find out the difference between chronological age and age estimated from brain MRI. The studies [12] shows that persons with PD can have higher white matter brain age gap than the grey matter brain age gap. The white matter and grey matter brain age gap in AD subjects is high when contrasted with the PD subjects. With help of RVM based regression [13] and using T1-MRI we could automatically inspect the brain age of healthy subjects.

I. Based on Resting-State Functional connectivity pattern

Functional Connectivity (FC) [14] can be used to effectively predict brain age from resting-state FMRI (rsFMRI) data. It allows to explore about development of brain and also various diseases which will inversely affect neuropsychiatry. Subject specific intrinsic connectivity networks (ICN) and voxel based measures of each ICN can be used to consolidate FC information into prediction of brain age. The expediency of rsFMRI data pave a way to predict brain age accurately.

J. Estimation from MRI and gender labels using TSAN.

Two-stage-age-network (TSAN) [15] can effectively estimate brain age of healthy controls from T1-MRI data. It introduced different novelties in prediction of brain age. Before predicting refined age, it will evaluate the brain age roughly. As TSAN is a cascade network, accurate brain age can be estimated from the rough brain age which is calculated before. A novelty here is that along with MRI it in take gender labels as input for better prediction.

## III.COMPARATIVE STUDY

The Table 1 describes a detailed study about the brain age prediction methods in past and their corresponding MAE (Mean Absolute Error) and Correlation between predicted age and chronological age.

TABLE 1. COMPARATIVE STUDY OF DIFFERENT BRAIN AGE PREDICTION MODELS.

| SL.No | Title | Author | Year of Publication | Model | MAE | Correlation (r) |
|---|---|---|---|---|---|---|
| 1 | Estimating the age of healthy subjects from T1-weighte MRI scans using kernel methods: Exploring the influence of various parameters [13] | K. Franke et. al | 2010 | SVR, Relevance Vector Regression | 5 years | r=0.92 |
| 2 | Predicting healthy older adult's brain age based on structural connectivity networks using artificial neural networks.[1] | Lan Lil et al | 2016 | Back Propagation Artificial Neural Network improved by Hybrid Genetic Algorithm(GA) and Levenberg-Marquardt(LM) Algorithm | 4.29 years | r=0.8 |
| 3 | "Predicting brain age with deep learning from raw imaging data results in a reliable and heritable biomarker".[2] | J. H. Cole et. al | 2017 | CNN | GM data: 4.16 years, raw data: 4.56 years | GM data: r=0.96, raw data: r=0.9 |
| | | | | GPR(Gaussian processes regression | GM data: 4.66 years | GM data: r =0.95 |
| 4 | Brain age prediction based on resting-state | H. Li, T. D Satterthwaite | 2018 | deep CNN | 2.15 years | r=0.614 |

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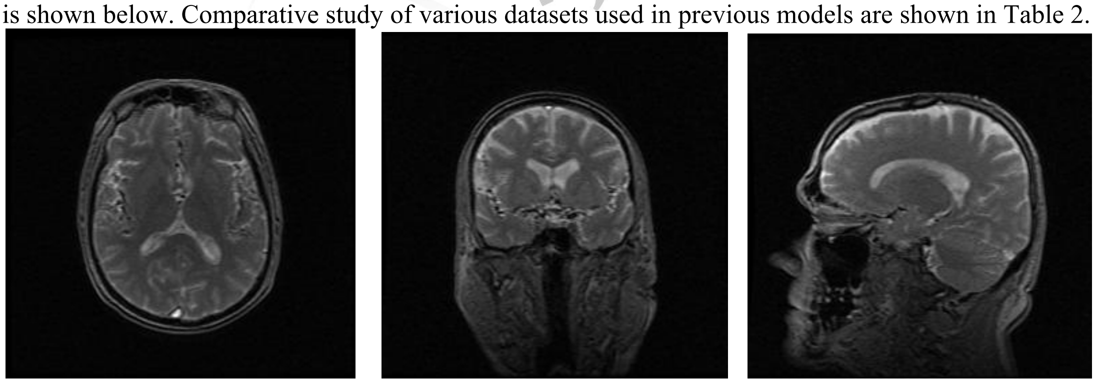
|---|---|---|---|---|---|---|
| | functional connectivity patterns using convolutional neural networks. [14] | et al | | | | |
| 5 | "Gray Matter Age Prediction as a Biomarker for Risk of Dementia".[4] | J. Wang et al | 2019 | CNN, Logistic Regression | 4.45 years | r=0.85 |
| 6 | "Multimodal brain-age prediction and cardiovascular risk: The Whitehall II MRI sub-study". [11] | A. M. G de Lange et.al | 2020 | XG Boost regressor | Mutimodal =3.37 | r=0.55 |
| | | | | | Grey Matter= 3.60 | r=0.46 |
| | | | | | White matter=3.51 | r=0.49 |
| | | | | | Functional Connectivity = 4.18 | r=0.04 |
| | | | | | External Gray matter = 10.69 | r=0.45 |
| 7 | "T1-weighted MRI-driven Brain Age Estimation in Alzheimer's Disease and Parkinson's Disease". [12] | I. Beheshti et.al | 2020 | Multivariate Machine learning Methods | Grey Matter = 3.60 | r=0.92 |
| | | | | | WhiteMatter = 4.85 | r=0.91 |
| 8 | Brain Age Estimation from MRI using a two-stage cascade network with ranking loss. [15] | Z. Liu et. al | 2020 | CNN | 2.428 years | r=0.985 |
| 9 | Accurate brain age prediction with lightweight deep neural networks. [3] | H. Peng et.al | 2021 | SFCN(Simple Fully Convolutional Neural Network) | 2.14 years | r= <0.1 |

## IV.DATASETS USED IN BRAIN AGE PREDICTION MODELS

Some of the widely used MRI datasets for brain age prediction are collected from Alzheimer's Disease Neuroimaging Initiative (ADNI), Open Access Series of Imaging Studies (OASIS), Predictive Analytics Competition 2019(PAC 2019), Information extraction from Images(IXI), International Consortium of Brain Mapping dataset (ICBM), Brain-Age Normative Control(BANC), Nathan Kline Institute-Rockland Sample (NKI-RS), Dallas Lifespan Brain Study (DLBS), Philadelphia Neurodevelopmental Cohort (PNC), Autism Brain Imaging Data Exchange (ABIDE), Consortium for Reliability and Reproducibility (CoRR), Parkinson's Progression Markers Initiative (PPMI) and UK Biobank. Fig.1 shows sample MRI images collected from Alzheimer's Disease Neuroimaging Initiative. T1 weighted MRI images in three planes axial, sagittal and coronal is shown below. Comparative study of various datasets used in previous models are shown in Table 2.



(a) (b) (c)

Fig.1. Sample ADNI dataset images in 3 planes : (a) Axial, (b) Coronal, (c) Sagittal

TABLE 2. COMPARATIVE STUDY OF DATASETS

| Sl.No | Title | Dataset | Age Range | No of Subjects |
|---|---|---|---|---|
| 1 | "Estimating the age of healthy subjects from T1-weighted MRI scans using kernel methods: Exploring the influence of various | T1 weighted MRI from IXI Database | 19-86 years | 550 healthy subjects |

| | | | | |
|---|---|---|---|---|
| | parameters". [13] | | | |
| 2 | "Age-related Classification and Prediction Based on MRI: A Sparse Representation Method". [6] | T1-weighted Structural MRI from ICBM | 19-79 years | 84 healthy volunteers |
| 3 | MRI-based age prediction using Hidden Markov models. [9] | T1 weighted MRI from ABSIS database | 50-86 | 20 healthy subjects |
| 4 | "Estimating brain age using high-resolution pattern recognition: Younger brains in long-term meditation practitioners". [8] | T1 MRI of meditators from area of Los Angeles | 4-46 | 50 Meditation practitioners |
| | | T1 MRI from ICBM database | 24-77 | 50 Control Subjects |
| 5 | "Predicting healthy older adult's brain age based on structural connectivity networks using artificial neural networks".[1] | T1w MRI | 50-79 years | 112 normal older subjects |
| 6 | "Predicting brain age with deep learning from raw imaging data results in a reliable and heritable biomarker".[2] | T1 weighted MRI from BANC | 18-90 years | 2001 healthy subjects |
| | | Individuals from UK Adult Twin Registry | Mean age : 61.86±8.36 years | 27 monozygotic twin, 4 dizygotic twins |
| 7 | Predicting brain-age from multimodal imaging data captures cognitive impairment.[10] | MRI from LIFE and NKI Rockland Sample | 19-82 | 2354 subjects |
| 8 | Predicting age from cortical structure across the lifespan. [7] | T1 MRI from IXI dataset | 20-86 | 427 healthy adults |
| | | T1 MRI from OASIS dataset | 18-94 | 314 healthy adults |
| | | T1 MRI from DLBS dataset | 20-89 | 315 healthy adults |
| 9 | Brain age prediction based on resting-state functional connectivity patterns using convolutional neural networks.[14] | rsfMRI scans from PNC dataset | 8-22 | 983 subjects |
| 10 | "Gray Matter Age Prediction as a Biomarker for Risk of Dementia". [4] | T1 w MRI from Rotterdam Study | Mean Age : 66±11 years | 3688 dementia free participants |
| 11 | "Investigating systematic bias in brain age estimation with application to post-traumatic stress disorders".[16] | T1 w , DTI, rsfMRI from ABIDE, CoRR, DLBS,NKI Rockland | 6-89 years | 2026 healthy subjects |
| 12 | "Multimodal brain-age prediction and cardiovascular risk: The Whitehall II MRI sub-study." [11] | T1 weighted, Diffusion weighted, FLAIR images, rsfMRI MRI from White Hall II imaging subsets | 60.34-84.58 years | 610 participants |
| 13 | "T1-weighted MRI-driven Brain Age Estimation in Alzheimer's Disease and Parkinson's Disease". [12] | T1 w MRI from IXI, OASIS , ADNI, PPMI | 35-90 years | 839 healthy controls |
| | | T1 w MRI from PPMI | Mean Age: 71.64±5.81 years | 160 PD patients |
| | | T1 w MRI from ADNI | Mean Age: 64.53±6.98 years | 129 AD patients |
| 14 | Brain Age Estimation from MRI using a two-stage cascade network with ranking loss. [15] | T1 w Structural MRI from ADNI, OASIS, PAC2019 | 17-98 years | 2001 subjects |
| 15 | Accurate brain age prediction with lightweight deep neural networks. [3] | T1 weighted MRI from UK biobank | 44-80 years | 12949 subjects |
| | | T1 Structural MRI from PAC 2019 | 17-90 years | 2638 subjects |

## V. DILEMMAS OF BRAIN AGE PREDICTION MODELS

Due to lack of samples [9] related to minimum and maximum age of subjects a comparative study is not possible. So there is a need for more prediction model with more accuracy. As the performance is evaluated it shows that it is highly dependent on size of the sample and age range of subjects [11]. For an accurate prediction voxel wise brain age will need large number of T1-weighted samples [12].

CNN models [4] are sometimes incapable of dealing with unaccustomed data samples for predicting brain age. Bias correction method [16] will not help in predicting brain age of subjects included in tethered age ranges. Large error will be associated with the prediction [ 15] when the data sample distributed is uneven.

Using multimodal data, it will enhance the brain age prediction when compared to resting state functional connectivity pattern [14]. CNN response in unavailability of common sense [5] is a major limitation. The under reckoning age in older individuals and over reckoning age in younger individuals is a major hindrance in the study [1].

## VI. FUTURE POSSIBILITIES OF BRAIN AGE.

Brain age can be used as a criterion for the neuro-diseases prediction. By using kernel methods [13] along with predicting neurodegenerative diseases it can be used as a biomarker for analyzing effects of drugs used in therapy. The relation of brain age to cognitive ageing [2] can be explored. Image derived biomarkers [11] can be effectively used to explore the effect in clinical factors for brain age prediction and this can be further upgraded to enhanced biomarker version. In patients with PD and AD, the relation of anxiety, depression and hallucination with brain age [12] can be evaluated which will be a novel future development.

## VII. CONCLUSION

In this paper, the different models used for brain age prediction in last 11 years is discussed. The comparative study of datasets used and brain age prediction models are also tabularized. The unaccustomed datasets and lack of data samples were the major limitations in the existing brain age models. Brain age can be used as a biomarker for prediction of diseases like Alzheimer's and Parkinson's and other various neurodegenerative diseases.

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