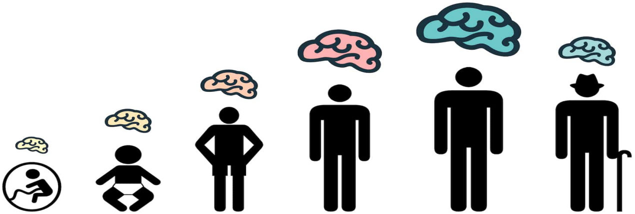
Brain Age Estimation from MRI-derived Features

Mansoor Ahmed

Lahore University of Management Sciences

Aging

Changes in structure and function of the body



Source: Neelam Sheikh

Brain Aging

Brain aging is characterized by changes at all levels, from molecules to structure, reflected by reduced brain size, altered vasculature, and declines in motor and cognitive features

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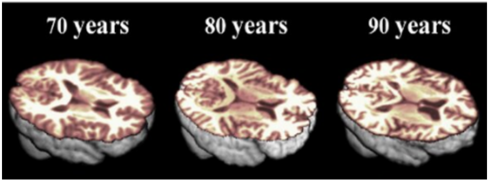
Canevelli and Marsili, 2022



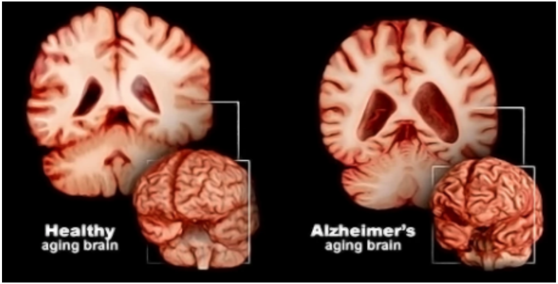
Source: David Alexander et al.

- Cortical thinning
- Change in white matter (WM) integrity
- Vascular changes

Neurological Disorders

Neurodegenerative Disorders

- Alzheimer's disease, Parkinson's disease, and schizophrenia



Source: TheVisualMD

- White matter reduced
- Cerebrospinal fluid increased
- Gray matter shrinked

Diagnosis of Neurological Disorders

- Invasive vs. non-invasive techniques
  - Anomalous anatomical structures
  - Abnormal brain activity

Source: Inspiring/Shutterstock

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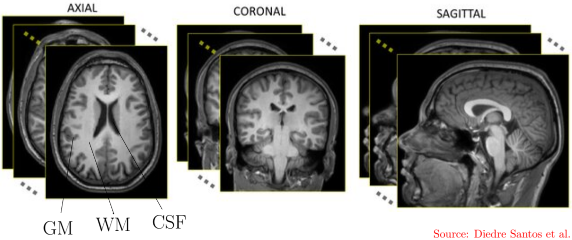
Motivation

- Types of Brain Aging
  - Chronological/Healthy Brain Aging
  - Biological Brain Aging
- Brain age gap (BAG) or Brain Estimated Age Difference (Brain-EAD)
  - Difference between chronological age and biological brain age
  - Neurodegenerative disorders - accelerated brain aging
  - Biomarker and proxy for brain health

"Accelerated or slower aging indicates an underlying neurological disorder."

Imaging: MRI

- Anatomical coordinate system (ACS)
  - Axial, Coronal, and Sagittal planes



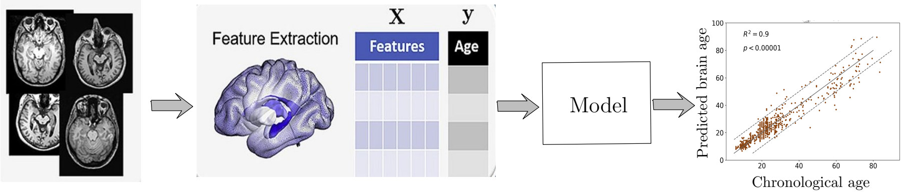
Source: Diedre Santos et al.

- T1-weighted MRI
  - Lower intensity - grey matter (GM) and cerebrospinal fluid (CSF)
  - Higher intensity - white matter (WM)

Problem Formulation

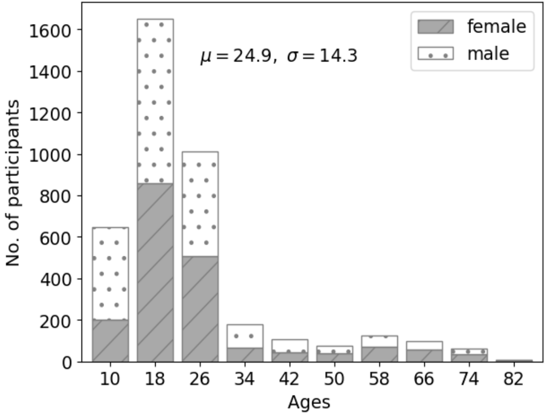
Given a brain MRI, predict its biological brain age

- Supervised learning problem
- Chronological ages as true labels - regression problem
- MRI-derived measurements as features
- Learn a brain age formula from healthy MRIs - machine learning
    - Healthy controls (brain age = chronological age $\implies$ BrainEAD = 0)



Dataset

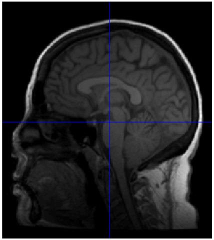
- Public benchmark dataset Open Big Healthy Brain (OpenBHB)[1]
  - Brain MRIs of 3985 healthy controls
  - 10 different sources with $>$ 60 individual MRI acquisition sites



[1]The dataset was provided (in part) by Neurospin, CEA, France.

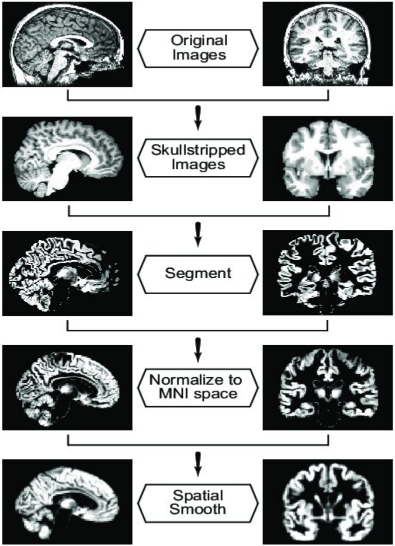
Preprocessing

- Undesired information - head, face, and non-brain tissue
- Different head sizes
- Noise - hyperintense or bright areas
- Different MRI scanners
- Head motion during a session



Preprocessing Pipeline

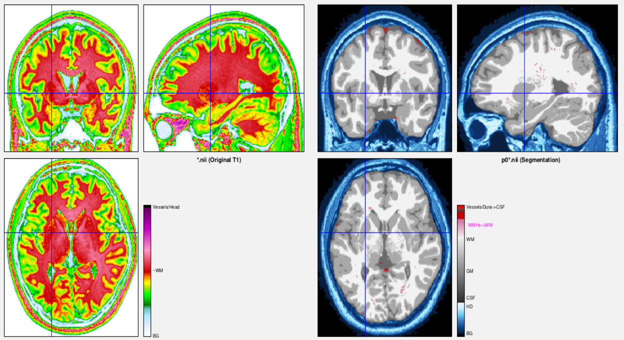
- Remove the skull
- Segment brain tissues
- Register to coordinate space
  - Standard MNI-152
- Perform smoothing



Source: Lin Yuan et al.

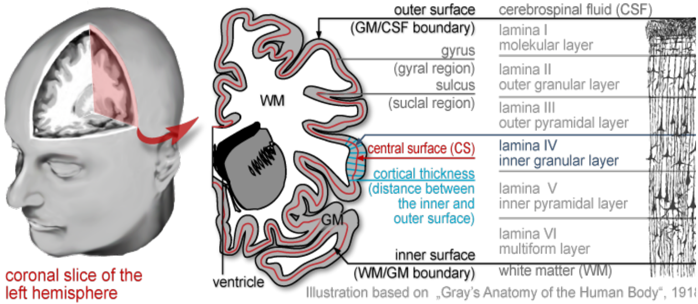
MRI Quality control

- CAT12 Automated Quality Control
  - Estimates the image resolution, noise, and bias
  - Highlights the hyper-intense regions
  - Computes an Image Quality Rating (IQR) score



Feature extraction: Using CAT12

- **Input:** The preprocessed MRI and a reference atlas (Parcellation)
  - Compares the input MRI with the parcellation
  - Divides the input MRI into parcels, aka regions of interest (ROI)
  - Computes the volumetric measurements for each parcel
  - Used a Neuromorphometrics atlas with a total of 284 whole-brain regions
- **Output:** Volumetric measurements of all ROIs



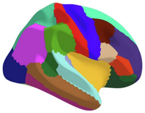
Source: CAT12 Manual

Feature extraction: Using FreeSurfer

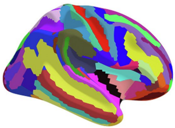
Only divides Gray Matter (GM)/cortex into ROIs

- **Input:** The preprocessed MRI and a cortical atlas
  - **Desikan atlas:**
    - A gyral based atlas: a gyrus includes the part visible on the pial view
  - **Destrieux atlas:**
    - Divides brain the cortex into gyral and sulcal regions
  - Computes the surface area (mm^2), GM volume (mm^3), cortical thickness (mm), and curvature (mm^{-1}) for each atlas
- **Output:** The region-wise measurements for each atlas

Desikan-Killiany atlas (Desikan et al., 2006)
68 ROIs, structural parcellation



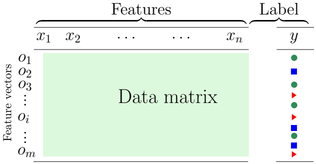
Destrieux atlas (Destrieux et al., 2010)
148 ROIs, structural parcellation



Source: FreeSurfer

Feature Representation

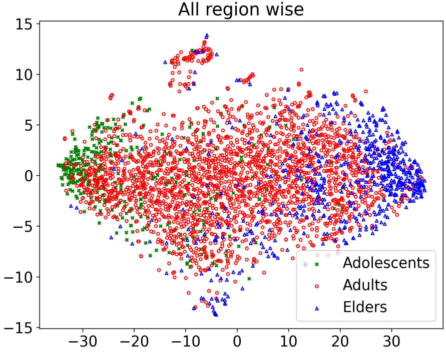
- Let $X^{m \times n} \in \mathbf{R}^{m \times n}$ be the data matrix with m being the number of subjects and n being the MRI-derived features
- Let $Y^{m \times 1}$ be their chronological ages



- Divide the participants into different age groups using k-means clustering, i.e., adolescents, adults, and elders

Feature Representation: *t*-SNE Visualization

- Features min-max normalized to bring the values between 0 and 1, $x_{scaled} = {}^{x - x_{min}}\!/_{x_{max} - x_{min}}$.
- Visualized the feature separation for the three age groups using t-distributed Stochastic Neighbor Embedding (*t*-SNE)
- "Adolescents" class (in green color) shows a separate group and is far away from the "Elders" class (in blue color)



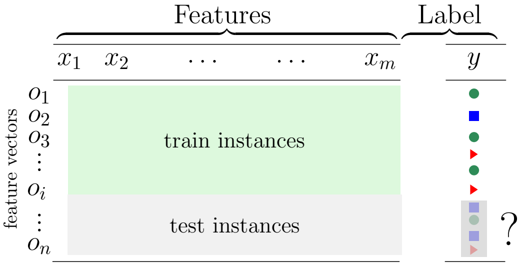
Working algorithm

Data: $X^{m \times n} \leftarrow$ Data matrix of m subjects, $Y^{m \times 1} \leftarrow$ chronological ages of m subjects.
Result: Let Y^{pred} be the estimated ages of m subjects.
for m subjects **do** $\triangleright$ Model training
    Train a regression model using the $X^{m \times n}$ with age labels $Y^{m \times 1}$
end for
Validate the prediction accuracy of the regression model $\triangleright$ Testing the regression model
Estimate the brain age Y^{pred} of HC testset

Sampling Approach

- $80 - 20\%$ random split to divide the data into training and testing sets with uniform gender distribution in both sets.
- The test set is further divided into male and female hold-out sets.

	Training set	Test set
No. of HC	3172	793
Age $\pm$ std (years)	25.2 ± 14.6	23.8 ± 12.8
Sex (M/F)	1661/1548	434/359



Model training

- Trained different regression models such as Support Vector Regression (SVR), Relevance Vector Regression (RVR), Linear Regression (LR), and Generalised Linear Model (GLM) to predict the brain age of the healthy test subjects. More formally:

  $$Y_m^{pred} = \beta_1 x_{m1} + \beta_2 x_{m2} + ... + \beta_n x_{mn} + c$$

  where β_1, β_2, and β_n are the unknown parameters while x_{m1}, x_{m1}, and x_{mn} are the selected brain MRI features.
- Fine-tuned the hyperparameters to optimize the model performance and prevent overfitting
- Trained the age estimation models using separate features, i.e., CAT12 and FreeSurfer (Desikan and Destrieux ROI)

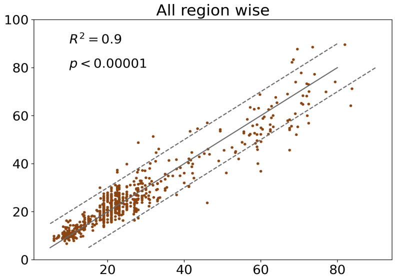
Results

- Using the standard metrics of mean absolute error (MAE), root mean squared error (RMSE), and R^2 score for evaluation
  - Lower MAE and RMSE and higher R^2 values indicate better model performance
  - Tested the model performance on gender-wise hold-out sets

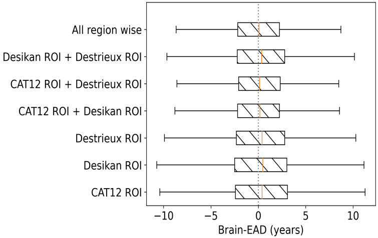
	Male			Female			Complete Data		
MRI features	MAE ↓	RMSE ↓	R^2 ↑	MAE ↓	RMSE ↓	R^2 ↑	MAE ↓	RMSE ↓	R^2 ↑
CAT12 ROI	3.9	5.68	0.86	4.17	6.11	0.81	3.94	5.32	0.87
Desikan ROI	4.39	6.93	0.79	4.03	5.69	0.83	4.23	6.4	0.81
Destrieux ROI	3.98	6.05	0.84	3.81	5.51	0.84	3.9	5.81	0.84
CAT12 ROI + Desikan ROI	3.29	4.94	0.89	3.54	5.11	0.87	3.4	5.02	0.88
CAT12 ROI + Destrieux ROI	3.24	4.78	0.90	3.44	4.97	0.87	3.33	4.87	0.89
Desikan ROI + Destrieux ROI	3.89	5.92	0.85	3.63	5.14	0.87	3.77	5.58	0.86
All region	**3.19**	**4.67**	**0.91**	**3.32**	**4.79**	**0.88**	**3.25**	**4.73**	**0.90**

Results: Visualization

- Chronological Age vs. Biological Brain Age



- Brain Estimated Age Difference (Chronological Age - Biological Brain Age)



Discussion

- All region-wise feature metrics from T1-w MRI improved the Brain Age Estimation (BAE) framework (lower MAE and RMSE than using individual feature metrics)
  - Seven cortical measurements or explanatory variables for brain regions using FreeSurfer improved the performance
- Integrating three region-wise structural measurements decreases brain-EAD
- GM volume shows a strong -ve correlation with age ($r \approx -0.5$), while CSF volume shows a strong +ve correlation with age ($r \approx 0.5$)
  - GM volume decreases with age, while CSF volume increases gradually with age
- Our model is **robust**:
  - Improved brain age estimation accuracy using region-wise features
  - Trained and tested on healthy samples with ages across the lifespan
  - Insights into the features contributing towards brain aging

Future research directions

- Include more adult and elder healthy training samples and explore the impact on the accuracy of the BAE model
- Use other global brain atlases, such as Suit and Cobra, other than the Neuromorphometrics atlas
- Integrate other modalities, such as functional MRI with MRI-derived region-wise features
- Ensemble brain age estimation models trained on different age groups
- Use the MRI volume, i.e., raw MRI, to train neural networks for brain age estimation

$$Thank\ You$$

Questions!!