Brain-age prediction: a systematic comparison of machine learning workflows

Shammi More[1,2,a], Georgios Antonoupolous[1,2], Felix Hoffstaedter[1,2], Julian Caspers[3], Simon Eickhoff[1,2] & Kaustubh R. Patil[1,2,b]

[1]Institute of Systems Neuroscience, Heinrich Heine University, Düsseldorf, Germany
[2]Institute of Neuroscience and Medicine (INM-7: Brain and Behaviour), Research Centre Jülich, Germany
[3]Department of Diagnostic and Interventional Radiology, University Hospital Düsseldorf , Germany
[a]s.more@fz-juelch.de, [b]k.patil@fz-juelich.de

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Introduction

- Estimate a person's age based on Magnetic resonance imaging (MRI) data
- **Brain-age delta = Predicted age – True age**
- Higher brain-age delta reflects poorer brain health[1,2].
- Impact of feature representations and machine learning (ML) algorithms is not known.
- **Aim:** Systematically evaluate 128 workflows by assessing:
  a. Within-site Performance
  b. Cross-site Performance
  c. Test-retest Reliability

Methods

128 Workflows = 16 Feature spaces × 8 ML algorithms

Voxel-wise: [(3 × 2 × 2) + 4]
- Smooth (S0, S4, S8)
- Resample (R4, R8)
- PCA (0,1)
- Schaefer's, Fan's & Buckner's atlases (1273, 873, 473, 173)

Parcel-wise

Ridge, Random Forest, Relevance vector-linear, Relevance vector polynomial, Kernel ridge, Gaussian process, LASSO, Elastic Net

Data: T1-weighted images from healthy subjects with a wide age range (18-90 years); **Training:** CamCAN, IXI, eNKI and, 1000brains[3-6] **Testing:** CoRR, OASIS-3, and ADNI[7-9]

Input features: Modulated grey matter images from Voxel-Based Morphometry[10] using CAT12.8 toolbox[11]

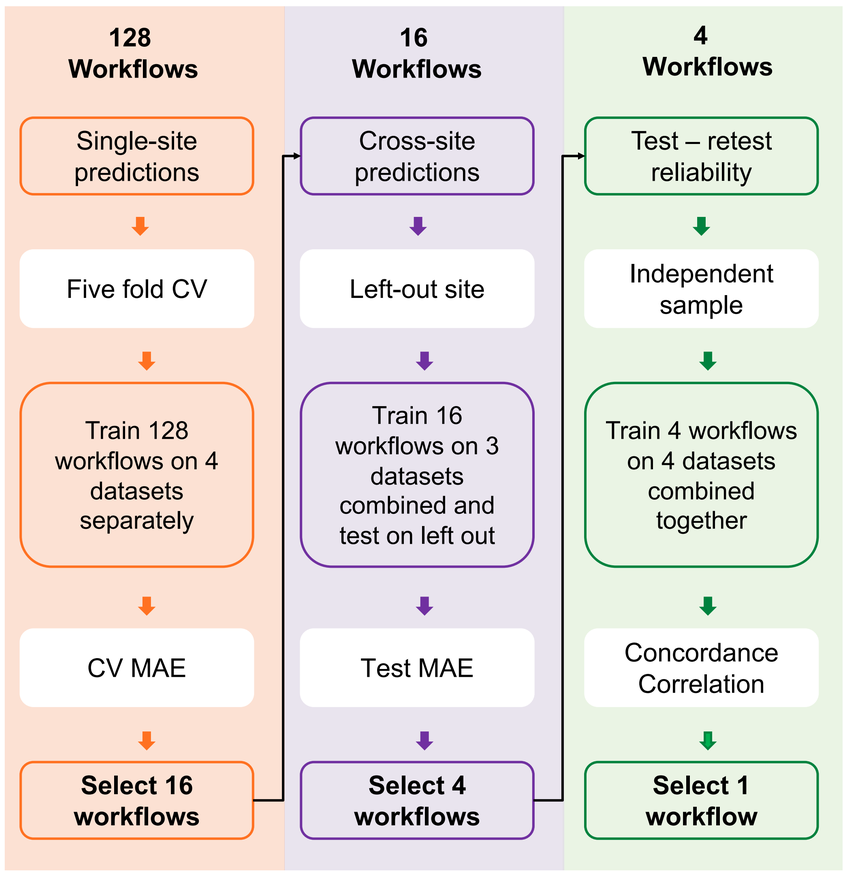


Figure 1. The framework to select the best workflow for brain-age prediction.128 workflows were first evaluated for their single-site prediction performance. Next, 16 workflows were selected based upon Cross-validation (CV) mean absolute error (MAE) and assessed for cross-site prediction performance. Then, four workflows were selected based on their test MAE and were assessed for test-retest reliability. The one best performing workflow was then selected.

Results

a. Within site evaluation

CV MAE: 4.9 to 8.5 years

Best workflow: S4_R4 + GPR

Feature space: Voxel-wise data smoothed with 4 mm FWHM and resampled to 4 mm

Model: Gaussian Process

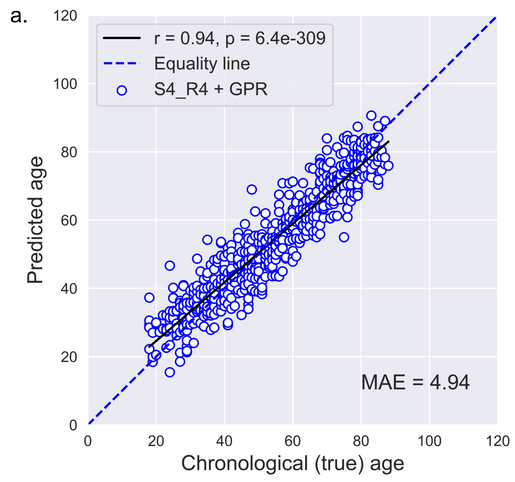
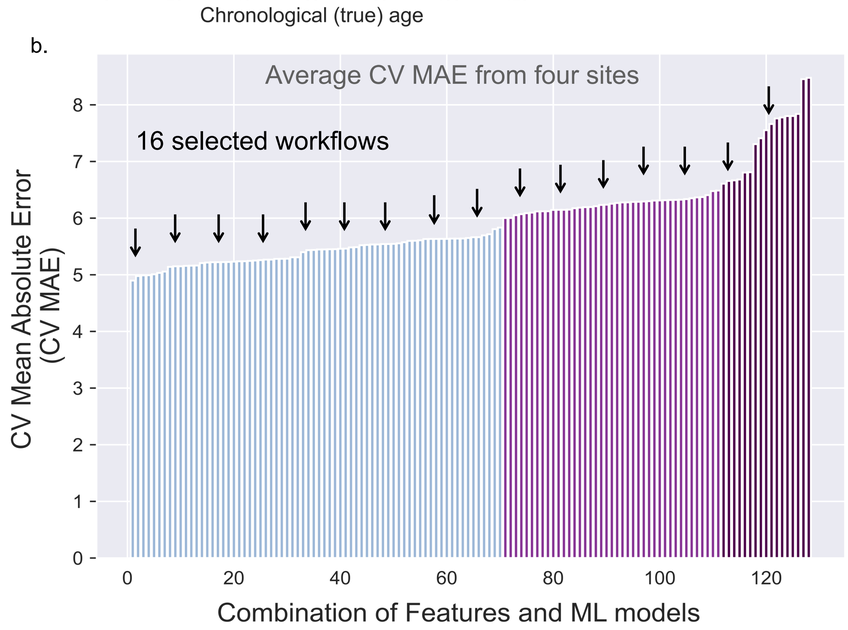


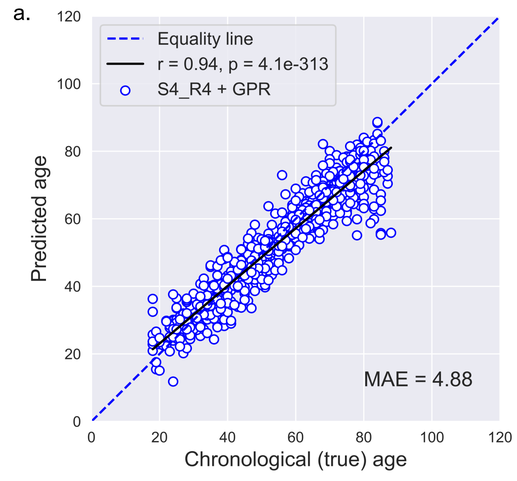
Figure 2. a. Scatter plot between true age and predicted age for CamCAN data. b. Averaged CV MAE arranged in the increasing order with arrows pointing to selected workflows.



b. Cross-site evaluation

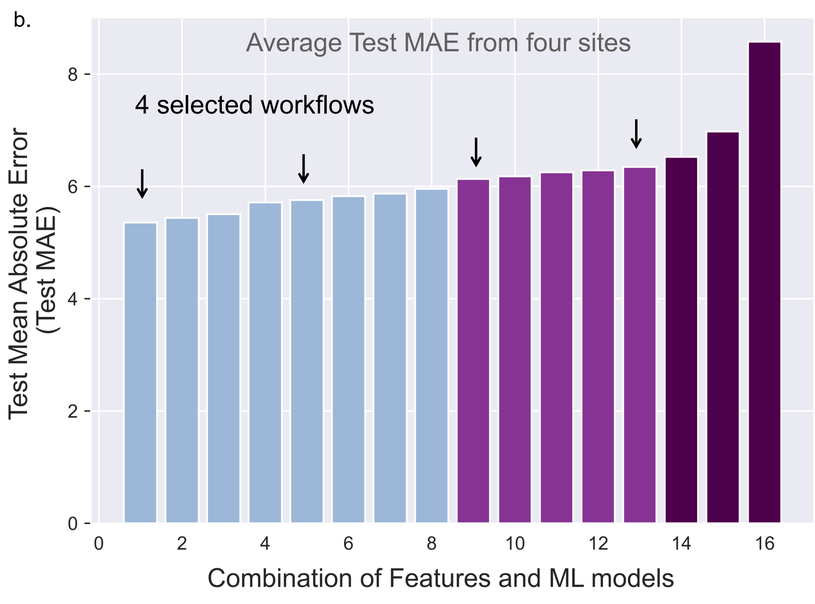
Test MAE: 5.4 to 8.6 years

Best workflow: S4_R4 + GPR



Same workflow selected from within-site and cross-site analysis

Figure 3. a. Scatter plot between true age and predicted age b. Averaged test MAE arranged in the increasing order with arrows pointing to selected workflows.



c. Test-retest reliability

- Four selected workflows trained using four datasets combined as training data
- CoRR dataset with two MRI scans per subject less than three months apart
- **Test-retest reliability:** Concordance Correlation Coefficient (CCC)[12]
- **Best workflow:** S4_R4 + GPR
- Brain-age estimations were stable: CCC = 0.97

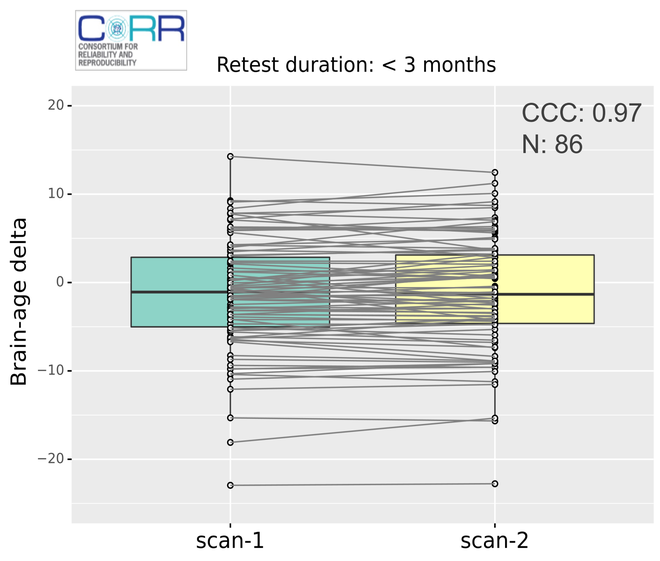
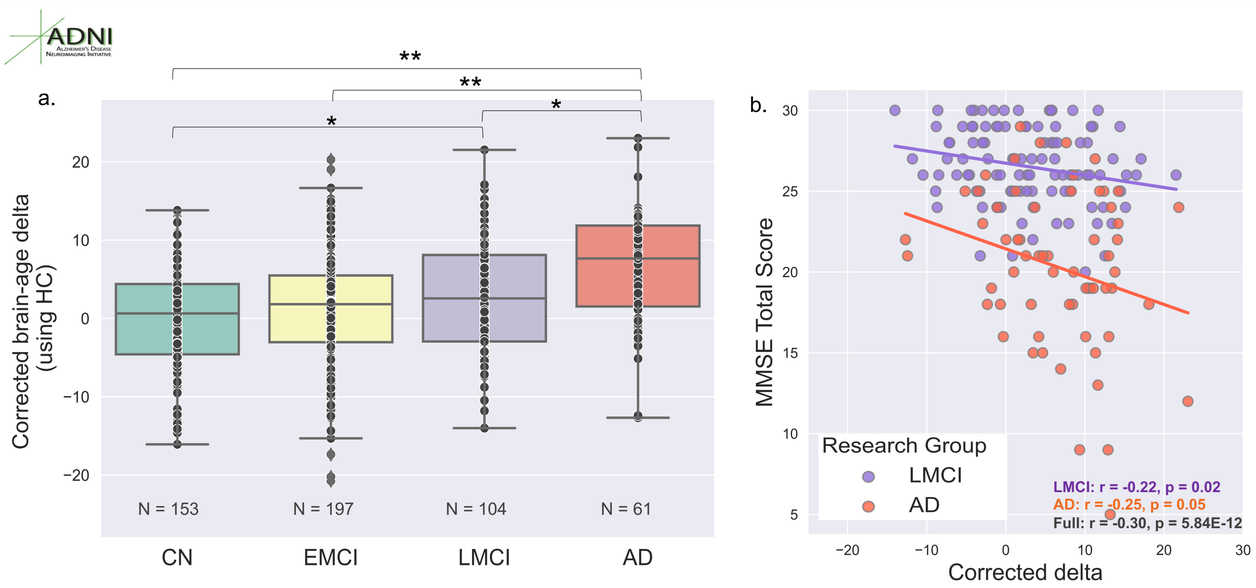


Figure 4: Brain-age delta from two time points of the same subjects with a retest duration of less than 3 months.

d. Application in Dementia



- Significantly higher delta in AD compared to CN, EMCI, and LMCI; and in LMCI compared to CN
- Negative correlation between MMSE and delta in AD and LMCI

Figure 5. a. Comparison of brain-age delta between cognitive normal (CN), early mild cognitive impairment (EMCI), late mild cognitive impairment (LMCI), & Alzheimer's Disease (AD). b. The scatter plot shows the correlation between corrected brain-age delta and Mini-Mental State Examination (MMSE).

Conclusions

- Effect of both feature representations and machine learning algorithms
- Voxel-wise data is better than parcel-wise data.
- Brain-age delta is reliable over a short duration of scan interval.
- Mean brain-age delta is higher in MCI and AD patients compared to CN, which is associated with higher cognitive impairment.

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