Predicting Brain Aging (Brain Age Gap) from Biomedical and Lifestyle Variables

Poster No:

1836

Submission Type:

Abstract Submission

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Introduction:

The Brain Age Gap (BAG) can be considered as an indicator of the brain health [1, 2]. BAG is defined as the difference between an individual's chronological age and the age predicted by a machine learning (ML) algorithm based on individual brain features. While some studies demonstrated univariate associations between the BAG and several lifestyle and biomedical variables [2, 3], a substantial gap persists in understanding the multivariate association between these factors and BAG. Here, we addressed this question by using a wide range of biomedical, lifestyle, and sociodemographic variables conjointly to predict the BAG in a large population of the UK Biobank.

Methods:

We built a ML model to predict an individual's brain age using brain structural features (cortical and subcortical parcellated grey matter volume) in a subset of specifically healthy participants in the UK Biobank (n =5,025, age range 46-82 years, 2,579 females). In particular, we applied ridge regression implemented in the Julearn package [4]. Subsequently, the optimized predictive brain model was applied to predict brain age in the remaining UK Biobank participants (n =34,365, age range 44-82 years, 18,128 females) (Fig 1A). The BAG was then computed following the adjustment of predicted brain ages for proportional bias based on regression parameters from the training set [5].
For predicting an individual's BAG, we selected 157 variables covering biomedical (e.g., cardiovascular, respiratory, and body metabolism), lifestyle (e.g. smoking and diet) and sociodemographic (e.g.: socioeconomical status, family and social life) variables in a subset of 7,736 participants not included in the healthy subset used to build the age prediction model (age range 44-81 years, 4,272 females). In order to train the model, we used a random forest algorithm as implemented in Julearn [4] with a nested cross-validation approach including 10 inner and outer folds. Notably, we controlled for possible confounds (age, age2, sex, height, and volumetric scaling from the T1 image to standard space).

Results:

We achieved a high level of accuracy in predicting chronological age using brain structural features. The average cross-validation Mean Absolute Error (MAE) of 3.75 years closely mirrored the MAE of the best model applied to the population data, which was 3.93 years and the correlation between chronological and predicted age was strong (r = 0.75 for the prediction model and 0.76 for the population data, Fig 1B). Using bias correction on the population's predicted brain age led to a relatively unbiased BAG with regards to age (Fig 1C). We then found that individual BAG could be robustly predicted to some extent by phenotypical variables with an average (across test folds) correlation between the predicted BAG and calculated BAG of 0.239±0.02, MAE of 4.54±0.10 years, and a Root Mean Square Error of 5.72±0.12 years. Examining mean features importance (Fig 2) further reveals that most features are relevant for the prediction. Nevertheless, biomedical factors, closely followed by lifestyle factors, appear to play a relatively more important role than sociodemographic variables.

Conclusions:

We successfully developed a brain age prediction model in a healthy sample that enables to compute brain age gap as a sensitive estimator of individual brain structural health in an aging population. Although the relationships between any individual factor and brain structural health can be seen as negligible based on previously reported effect sizes [6], here we showed that considering a range of variables jointly enables a decent prediction of BAG. Although no set of variables appear to play a crucial role here, biomedical factors related to body metabolism and cardiovascular systems, as well lifestyle factors directly influencing these later (such as smoking and alcohol consumption) appear relatively important for structural brain health.

Lifespan Development:

Aging [1]
Normal Brain Development: Fetus to Adolescence
Lifespan Development Other

Modeling and Analysis Methods:

Classification and Predictive Modeling
Multivariate Approaches [2]

Keywords:

Aging
Cortex
Data analysis
Data Registration
Machine Learning
Multivariate
Phenotype-Genotype
Sub-Cortical
Other - Uk Biobank

[1|2]Indicates the priority used for review

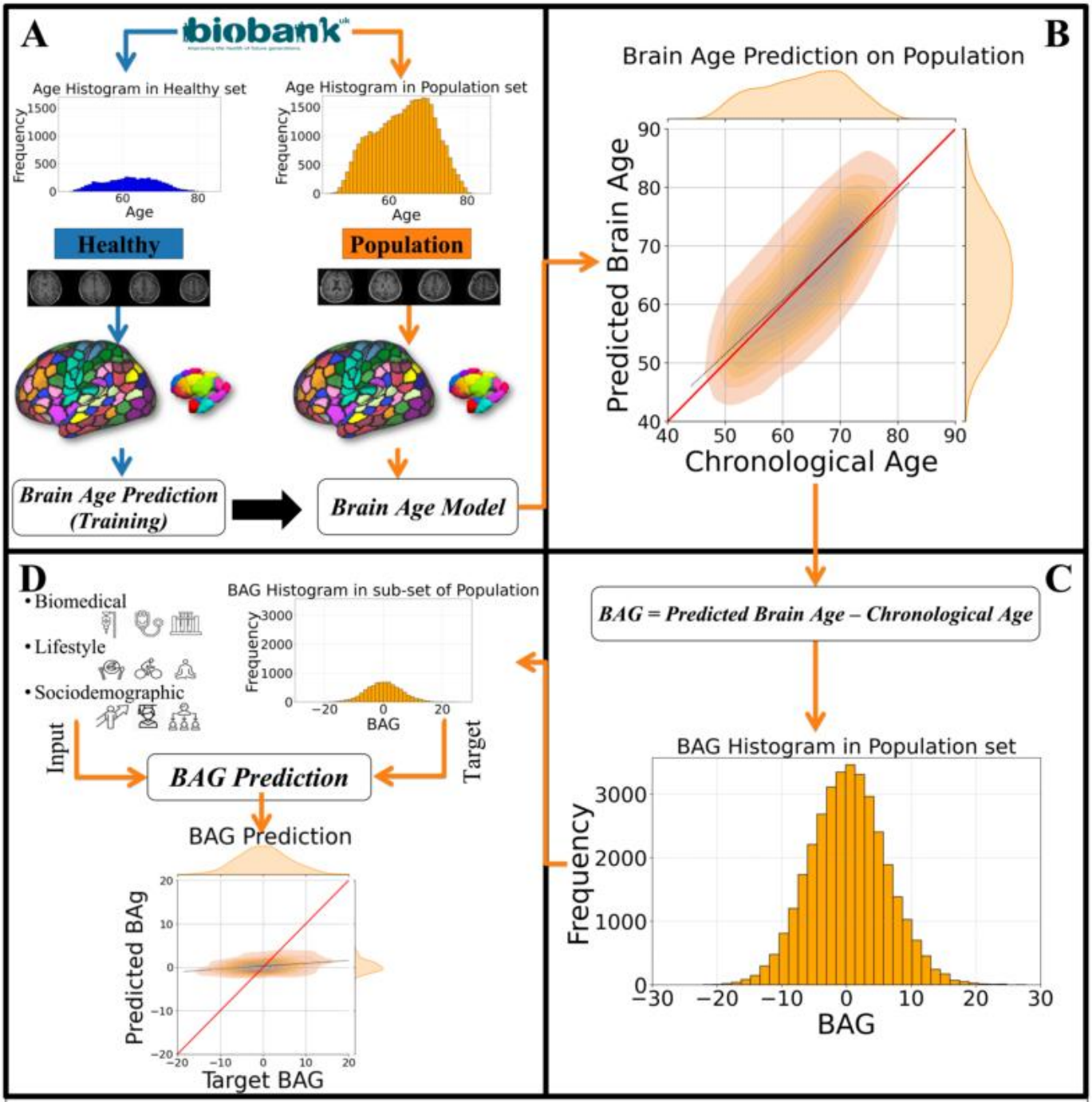

Fig 1. (A) Brain Age Prediction: After dividing the whole UK Biobank cohort into healthy and target population sub-sets, the healthy sub-set was used to design the Brain Age prediction model. In this model, Gray Matter Volumes (GMVs) of different cortical and subcortical brain parcels were used as feature inputs and chronological ages as target. Then GVMs of the population sub-set were used to predict the population's brain ages. **(B) Predicted Brain Age Vs Chronological/True Age** after bias correction; the red line is the identity line and the black dotted line is the best-fitted line based on joint scatter distribution of predicted and true ages. **(C) BAG Calculation:** By subtracting chronological/true ages from bias-corrected predicted ages Brain Age Gap (BAG) can be calculated; As shown here, some participants have positive BAG which means their brain is older than their true age while some have negative BAG. **(D) BAG Prediction:** A wide range of variables mainly in biomedical, lifestyle, and sociodemographic categories were used conjointly to predict the BAG in 7735 UK Biobank participants.

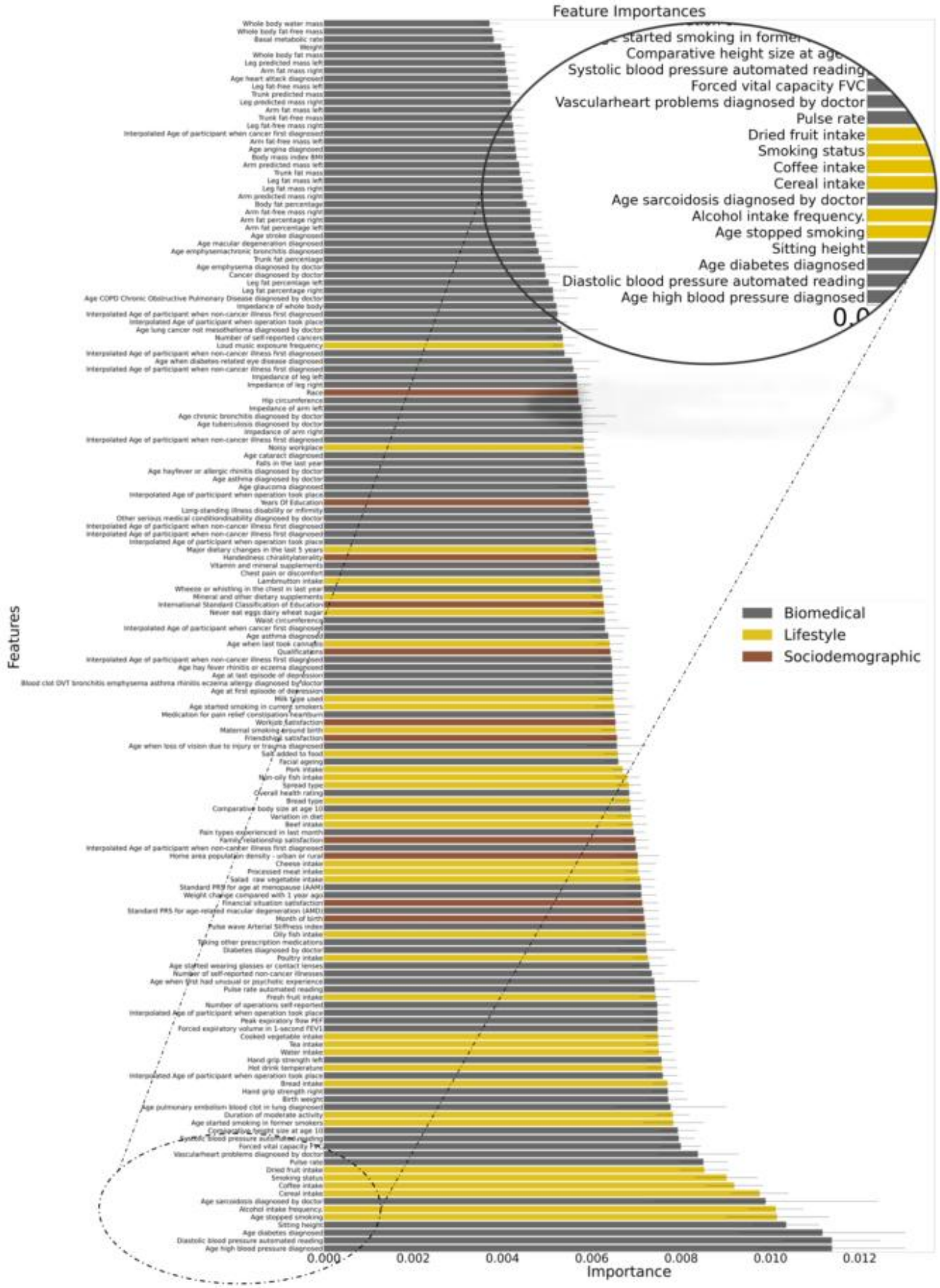

Fig 2. Mean features' importance across the outer folds for the BAG prediction: The use of random forest ML model allows us to examine the importance of features in predicting BAG based on the reduction of impurity criterion. Error bars represents standard deviation across folds.

Abstract Information

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No

Please indicate below if your study was a "resting state" or "task-activation" study.

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Healthy subjects only or patients (note that patient studies may also involve healthy subjects):

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Was any human subjects research approved by the relevant Institutional Review Board or ethics panel? NOTE: Any human subjects studies without IRB approval will be automatically rejected.

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Please indicate which methods were used in your research:

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Behavior
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For human MRI, what field strength scanner do you use?

3.0T

Which processing packages did you use for your study?

SPM
Other, Please list - CAT12, JuLearn (python package)

Provide references using author date format

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