# Characterizing brain age in the Alzheimer's disease connectome project (ADCP) using a deep neural network pre-trained on the UK Biobank

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Nagesh Adluru[1], Veena A. Nair[1], Vivek Prabhakaran[1], Vishnu Bashyam[2], Shi-Jiang Li[3], Ozioma Okonkwo[1], Richard J. Davidson[1], Andrew L. Alexander[1], Barbara B. Bendlin[1]

[1]University of Wisconsin, Madison, [2]University of Pennsylvania, Philadelphia, [3]Medical College of Wisconsin, Milwaukee

In the AD connectome project, the (median) excess aging of the brain, estimated using a publicly available deep learning model pre-trained on the UK Biobank, is about a year in the AD group and about half a year in the MCI group.

## INTRODUCTION

Overall age of an individual is commonly measured in chronological time. With the advent of in vivo imaging and reliable predictive modeling, a finer gradation of age into many internal biological scales such as cellular, tissue, organ and cognitive aging etc. can be estimated.

Accurate estimation of the age of the in vivo brain can offer insights into its differential aging patterns and accelerated excess aging due to the burden of disease processes eventually leading to dementia. Modern machine learning algorithms have allowed for accurate estimation of "brain age" using MRI data at an individual level. This is in contrast and complementary to population level statistical parametric maps of age effects on the brain.

The purpose of this study was to evaluate the applicability of a 3D fully convolutional neural network (FCNN), pre-trained on a large dataset of over ten thousand T1-weighted (T1-w) MR images from the UK Biobank to data from the Alzheimer's disease connectome project (ADCP).

**Code availability:** Minimal transformations and post-prediction analysis code available at https://github.com/nadluru/aaic2021. The prediction itself was based on publicly available code from another GitHub repository[3].

## METHODS

T1-w MRI data acquired from 152 participants were minimally transformed to strip the non-brain tissue, reduce B1 field bias using N4 algorithm in ANTS[1], and linearly registered to standard MNI T1w-template using FSL[2]. These images were then input to the pre-trained FCNN (without additional training) to predict their brain age[3]. A linear regression between calendar age and brain age gap with leave one out folds of the data was used to correct the bias in each of the predicted brain age[4].

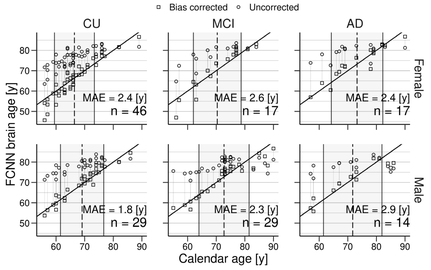


**Figure 1.** Predicted brain age by FCNN and calendar age for each of the three groups and two sexes. The bias correction procedure brings the predicted brain age of the samples closer to the unit slope and zero intercept line. The sample size and mean absolute error (MAE) in prediction after bias correction are shown on the bottom right of each sub-plot. Mean and one standard deviation spread of the calendar age are also shown.

## RESULTS

The brain age predictions before and after bias correction, mean and spread ($\sigma$) of the calendar ages, mean absolute error of prediction for each group and sex are shown in **Fig. 1**. The quantiles of the excess aging of the brain i.e., gap between the bias corrected brain age and calendar age are shown as Tukey box plots in **Fig. 2**.

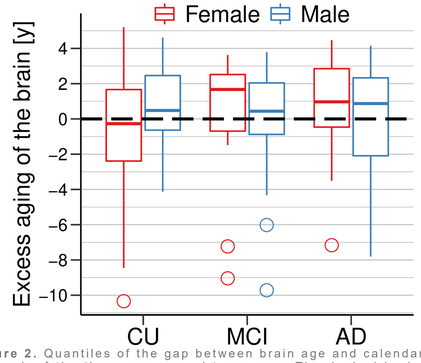


**Figure 2.** Quantiles of the gap between brain age and calendar age for each of the three groups and two sexes. The dashed horizontal line represents no gap between calendar age and the brain age. When averaged over the sexes, the median excess age of the brain in years for the three groups is: CU (0.0), MCI (0.6), and AD (0.9). It is also interesting to note that the excess brain aging for the females is higher than that in the males for the MCI but not AD group (given the evidence that AD affects women more than men).

## CONCLUSIONS

With a minimal set of transformations of T1w-MRI data, the UK Biobank pre-trained deep neural network (DNN), along with a linear bias correction, provided an estimate of the age of the brain in ADCP with a very good approximation. The analysis revealed that the median gap between the brain age and calendar age is about a year in the AD group, and about half a year in the MCI group and none in the CU group when averaged over the sexes. This provides preliminary evidence of accelerated aging of the brain in the cognitively impaired groups (MCI and AD).

Future analyses involve examining excess brain and cognitive aging due to amyloid and tau burden. The brain age prediction by the DNN had significant regression to the mean bias. This bias can be effectively corrected post-prediction with a simple linear regression. Future work entails investigating alternative bias correction methods and developing DNNs that can avoid such a bias intrinsically thus improving generalization, standardization, and individualized precision of such predictive models.

## REFERENCES

1. Avants, B. B., Tustison, N., & Song, G. (2009). Advanced normalization tools (ANTS). Insight j, 2(365), 1-35.

2. Jenkinson, M., Beckmann, C. F., Behrens, T. E., Woolrich, M. W., & Smith, S. M. (2012). Fsl. Neuroimage, 62(2), 782-790.

3. Peng, H., Gong, W., Beckmann, C. F., Vedaldi, A., & Smith, S. M. (2021). Accurate brain age prediction with lightweight deep neural networks. Medical image analysis, 68, 101871. (GitHub: https://github.com/ha-ha-ha-han/UKBiobank_deep_pretrain).

4. Beheshti, I., Nugent, S., Potvin, O., & Duchesne, S. (2019). Bias-adjustment in neuroimaging-based brain age frameworks: A robust scheme. NeuroImage: Clinical, 24, 102063.

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