Deep Learning Methods for Estimating "Brain Age" from Structural MRI Scans

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Abstract

Discrepancies between the chronological age of an individual and the neuroimaging based data driven "brain age" have been shown to be feasible biomarkers associated to a wide range of neurological disorders such as Alzheimer's Disease, traumatic brain injuries or psychiatric disorders. We devised a framework based on Deep Gaussian Processes which achieves state-of-the-art results in terms of global brain age prediction. We also introduced the first ever attempt of predicting brain age at voxel-level using context-sensitive Random Forests. The resulting models provide feasible brain-predicted age estimates for younger to middle-aged subjects, with less reliable estimates for older subjects.

1 Introduction

In 2009, there were an estimated 36 million people living with dementia, with numbers forecasted to double every twenty years. Old age is associated with increased probability of developing neurodegenerative diseases such as Alzheimer's Disease or Dementia. Consequently, a huge emphasis in the medical community is on detecting this life-threatening diseases at an early stage.

Chronological age alone is not a good predictor of disease risk, hence a data-driven metric derived from neuroimaging data could provide a more accurate predictor for future health outcomes. To model differences in age-related brain structure, we used a machine-learning based approach to generate a 'brain-predicted age' value from patterns of volumetric data contained in T1-weighted MRI scans [1].This technique defines a regression model of healthy brain ageing based on scans from a large independent healthy sample, which allows accurate prediction of age in new individuals. The difference between brain-predicted and chronological age has previously been shown to be sensitive to changes after a traumatic brain injury or Alzheimer's Disease [1,2]. While a neuroimaging derived 'brain-predicted age' measure is useful, we can argue that it does not offer enough discriminative information as to actually inform what possible neurodegenerative diseases will most likely commence. Therefore, devising a voxel-level brain-predicted age framework would transmit more information to clinicians.

2 Materials

2.1 Subjects

For training our algorithms we used a pooled dataset stemming from multiple sites, which we denote as Brain Age Normative Control (BANC), composed of 2001 healthy individuals with a male/female ratio of 1016/985, with a mean age of 36.95 ± 18.12. The participants in the study have an age range between 18-90 years.

For the purpose of testing the generalization power of our approach, we use The Cambridge Centre for Ageing and Neuroscience (Cam-CAN) dataset consisting of 653 T1 MRI scans with the subjects

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having an age range of 18-88 years. All of the neuroimaging data was acquired either at 1.5t or 3T using standard T1-weighted sequences.

2.2 Data preprocessing

All MRI scans were preprocessed using the Statistical Parametric Mapping (SPM12) software package . This entailed tissue segmentation into gray matter (GM) and white matter (WM), followed by a nonlinear registration procedure using the DARTEL algorithm [3] to the Montreal Neurological Institute 152 (MNI152) space, subsequently followed by resampling to $1.5mm^3$ with a 4mm smoothing kernel.

3 Methods

3.1 Deep Gaussian Processes

Deep Gaussian Processes (DGP) [4] can be interpreted as a multi-layer hierarchical generalization of Gaussian Processes. In contrast to Deep Neural Networks, DGP have mappings between layers which are governed by Gaussian Processes (GP). Therefore, they retain the nonparametric modelling power of GP and also propagate through the hierarchy the predictive uncertainties of a regular GP. Additionally, it can also learn layers of increasingly higher abstraction due to its deep structure.

3.2 Context-Sensitive Random Forests

Random Forests with Context-Sensitive (RF-CS) features have been successfully used for segmentation of brain tumor tissues [5].

To estimate the *brain-predicted age* at every voxel, we devise context features consisting of the intensity value of the voxel alongside 10,000 random features of the following type: mean or variance of voxel intensities present in a block of randomly sampled size and random offset compared to the initial voxel location, respectively taking two of the aforementioned features and subtracting them.

4 Results

4.1 Global-level Brain Age Prediction

Our DGP has an architecture consisting of 1 hidden layer with 2 hidden units and 20 pseudo-inputs at each level of the hierarchical architecture. We obtained a mean absolute error (MAE) of 3.85 years on the testing set of BANC using both gray matter and white matter. The best GP model on the same testing set achieves a MAE of 4.44 years.

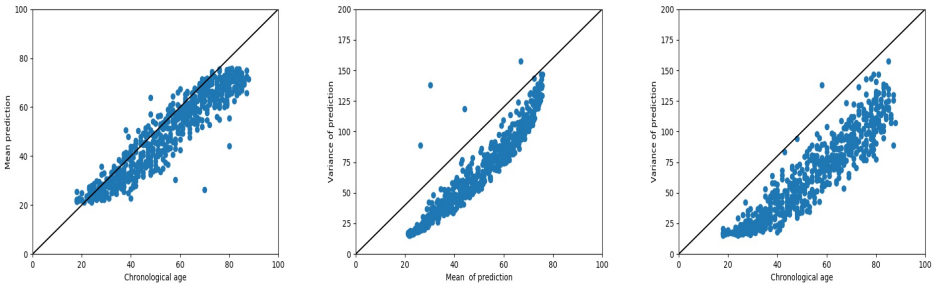
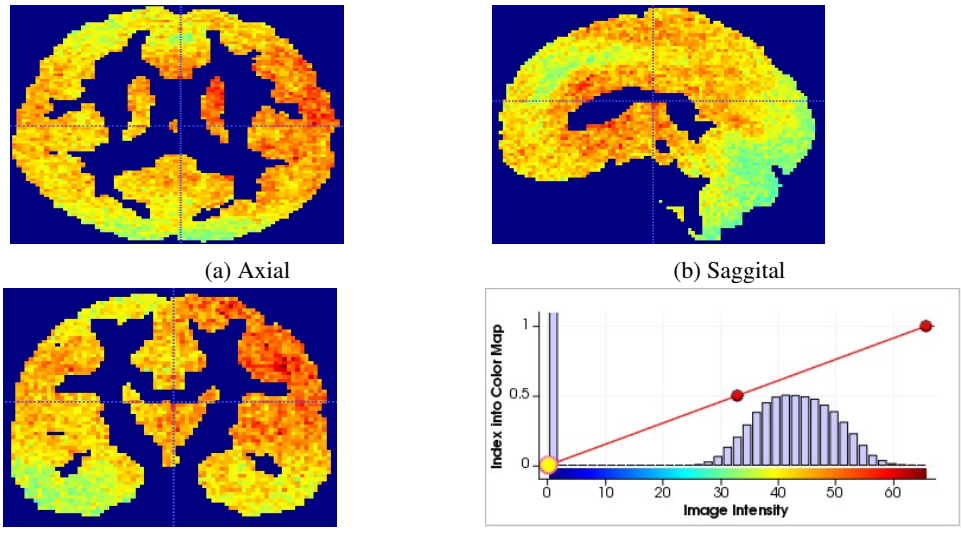


Figure 1: Relationships between predictive mean, predictive variance and chronological age on Cam-CAN

To test the generalization properties of our algorithm, we repeat the analysis on the external dataset, Cam-CAN. Figure 1 illustrates that the performance degrades as the subjects are getting older. Predictive uncertainty exhibits an almost positive linear relationship with the chronological age of the subjects.

4.2 Voxel-level Brain Age Prediction



(a) Axial (b) Saggital

(c) Coronal (d) Color bar

Figure 2: "brain-predicted age" estimates at voxel-level using RF-CS with GM volumetric data for a subject aged 61; d) histogram of "brain-predicted age" values for entire brain

Using RF-CS we obtain a mean MAE (mMAE) value taken over all voxel locations of 8.36 years on the testing set of BANC. Lower mMAE values were detected near the ventral areas of the brain, whereas for the cerebellum we obtained higher mMAE values. In Figure 2 we can notice the spatial variation of the underlying ageing mechanism for a subject aged 61.

5 Discussion and Future Work

In this paper, we introduced a novel deep learning framework for estimating global *brain-predicted age*. The framework demonstrated high accuracy for young to middle aged individuals, with the model being increasingly more uncertain in its predictions for older subjects. Feasible explanations include the fact that our training set is biased towards younger subjects. Besides that, increasingly more heterogeneous ageing patterns might be present as subjects age which might possibly affect accuracy. The same problems were also noticed for predicting *brain-age* at voxel-level. Nevertheless, the presented voxel-level model represents a stepping stone in the prospective usage of "brain-predicted age" as a region-of-interest biomarker in detecting a wide range of neurodegenerative diseases.

For future work, we are planning on extending the DGP framework with convolutional kernels, which would be better suited for imaging data in comparison to currently used squared exponential kernels. Lastly, we are expecting an increase in accuracy by using Dilated Convolutional Neural Networks (CNN) instead of Random Forests for predicting *brain-age* at voxel level.

References

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