

# Machine learning models of brain ageing in health and disease

Cole, J.H.<sup>1</sup>

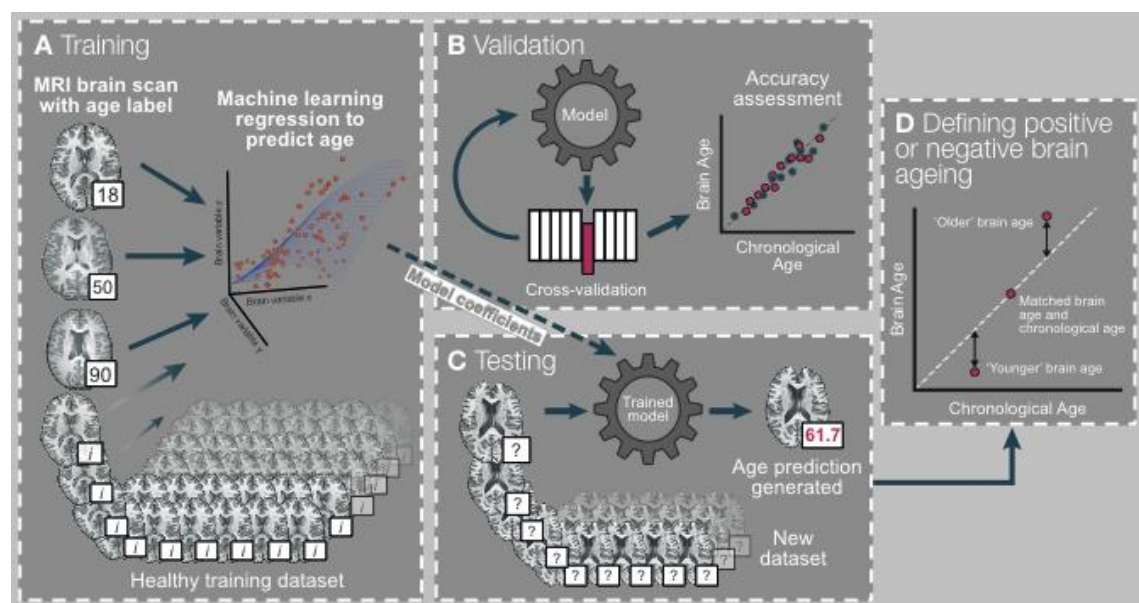
<sup>1</sup>Department of Neuroimaging, Institute of Psychiatry, Psychology & Neuroscience, King's College London.

## 1. Background

The brain changes as we age, and these changes are associated with cognitive decline and an increased risk of dementia (Deary *et al.*, 2009). Neuroimaging can measure these age-related changes, and considerable variability in brain ageing patterns is evident (Raz and Rodrigue, 2006). Equally, rates of age-associated decline affect people very differently. This suggests that the measurement of individual differences in age-related changes to brain structure and function may help establish whether someone's brain is ageing more or less healthily, with concomitant implications for future health outcomes. To do this, research into biomarkers of the brain ageing process is underway (Cole and Franke, 2017), principally using neuroimaging and in particular magnetic resonance imaging (MRI).

## 2. Overview

Here I will present my development of a brain-ageing biomarker, so-called 'brain-predicted age', derived using machine learning analysis of structural MRI data. I will outline the analytic pipeline involved (Figure 1), before going on to present results on the application of this biomarker to studies of the general population and outline some insights gained from studying brain ageing in specific diseases. These diseases include Down's syndrome, HIV, traumatic brain injury, epilepsy, multiple sclerosis and Alzheimer's. Finally, I will talk about ongoing developments, including my work on modelling brain ageing using multi-modality MRI data.



**Figure 1** Overview of the brain age prediction process using supervised machine learning,

*taken from Cole & Franke (2017) (A) Neuroimaging data, usually T1-weighted structural MRI scans, from healthy individuals (training set) are labelled with the participants' chronological age and put into a machine learning regression model. (B) To validate the accuracy of the model, a proportion of the participants' images are left out using e.g., tenfold cross-validation. (C) The model is trained using the entire training set and the resulting model coefficients are applied to new participants' brain scans (test set) to generate unbiased individual brain age predictions. (D) The predicted brain age can then be compared with the chronological age of test-set participants, with 'older'-appearing brains assumed to reflect advanced brain ageing and 'younger'-appearing brains to reflect decelerated or healthy brain ageing. The discrepancy between brain age and chronological age (brain-predicted age difference) can then be used as a metric to statistically relate to other measured characteristics of the participants.*

### **3. Conclusions**

Brain ageing can be accurately measured using structural MRI, thanks to its sensitivity to brain volume changes, indicative of atrophy. By modelling brain ageing in healthy people, the brain-predicted age of a single individual can be quantified. Having an older-appearing brain is common in people with neurological or psychiatric disorders. Moreover, the extent to which an individual's brain appears older than their chronological age relates to cognition performance, future clinically-relevant changes and even general health outcomes such as life expectancy.

### **4. References**

Cole JH, Franke K. Predicting Age Using Neuroimaging: Innovative Brain Ageing Biomarkers. *Trends in neurosciences* 2017; 40 12: 681-90.

Deary IJ, Corley J, Gow AJ, Harris SE, Houlihan LM, Marioni RE, *et al.* Age-associated cognitive decline. *Br Med Bull* 2009; 92(1): 135-52.

Raz N, Rodrigue KM. Differential aging of the brain: patterns, cognitive correlates and modifiers. *Neuroscience and biobehavioral reviews* 2006; 30(6): 730-48.