CM3203 One Semester Individual Project – 40 credits

Initial Plan: Predicting Brain Age from MRI Data Using Convolutional Neural Networks

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February 7th, 2021

Project Description

Ageing has a direct structural impact on the brain that correlates with decreased mental and physical fitness. As we age, the brain experiences some natural physical changes: reduced brain volume (especially in prefrontal cortex), shrinking of grey and white matter, reduced volume of striatum, temporal lobe, cerebellar vermis, cerebellar hemispheres and hippocampus (Peters, 2006). Findings also suggest that men and women experience more brain deterioration in different areas i.e., frontal and temporal lobes are more affected in men as opposed to the hippocampus and parietal lobes in women (Peters, 2006).

Increased brain age frequently poses a risk of neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease, as well as higher mortality rates (Levakov *et al.*, 2020). Often, when cognitive decline becomes obvious, it is too late to treat it adequately. Having a method to predict brain age would be a good indicator of early signs of brain deterioration which would allow to treat abnormalities before any symptoms become visible.

Over the recent years, machine learning techniques have enabled automatic disease prediction from imaging data. The aim is to increase the prediction accuracy beyond human performance to assist in clinical diagnosis and treatment decisions. The predicted age from these techniques can be considered to be the "brain age" because it is purely derived from the imaging data. However, it is not just the brain age that it is relevant, it is the difference between the predicted age and the actual age – known as brain-age delta – that matters. This value can provide very valuable insight into the ageing speed of an individual. A positive delta implies that a subject's brain looks older than their real age, meaning they are experiencing accelerated ageing (Peng *et al.*, 2021). Here, brain-age delta acts as an effective biomarker and is able to show differences between clinical groups (Kaufmann *et al.*, 2018), and is predictive for mortality (Cole *et al.*, 2018). Thus, it is of high importance to generate accurate brain age predictions as an essential pre-requisite for considering brain-age delta as a biomarker.

Numerous studies strive to reach the goal of making the most accurate brain age prediction system. Some of the methods used in the literature include machine learning methods such as linear regression, support vector machines and Gaussian process regression (Dosenbach *et al.*, 2010; Gaser *et al.*, 2013; Aycheh *et al.*, 2018; Liang, Zhang and Niu, 2019; Da Costa, Dafflon and Pinaya, 2020) and more recently, deep learning techniques (Cole *et al.*, 2017; Kawahara *et al.*, 2017). However, brain age prediction accuracy still needs further improvement, especially in smaller datasets where there is not enough data to train the model (Peng *et al.*, 2021). Also, some research suggests that deep learning performs no better than simple machine learning models in neuroimaging datasets (He *et al.*, 2020).

Traditionally, brain age prediction was performed by extracting features from brain MRIs, followed by classification or regression analysis (Jonsson *et al.*, 2019). A disadvantage of such feature extraction methods is the loss of information since the features are not explicitly for extracting information related to brain age. Nowadays, deep learning methods like convolutional neural networks (CNNs) can learn features that are important without a bias or a hypothesis (Jonsson *et al.*, 2019).

This project will implement a 3D Convolutional Neural Network trained on T1-weighted MRIs from the Cam-CAN dataset, inspired on the structure implemented by Cole *et al.* (2017) shown in *Figure 1*.

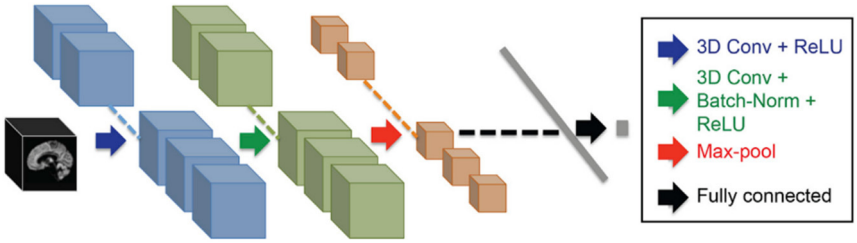

Figure 1 CNN architecture implemented by Cole *et al.* (2017)

The proposed structure for this project will have five layers, four of them to be used for feature extraction and the last layer with a constrained regression model (Treder, 2020; Treder *et al.*, 2021) to reduce bias. The model will be evaluated to measure how successful it is at predicting variables from the given data by measuring the mean absolute error (MAE) and the mean squared error (MSE). Cross-validation will be used to split the dataset into subsets and perform an analysis on one subset at a time. Data is split into two sets: training and test. The training set is used to train the model, while the test set is used to measure how well the model performs at making predictions on that test set. For the purpose of reducing variability of results, ten rounds of cross-validation will be carried out using different portions of the dataset.

Ethics

The data for this project has been provided by Cam-CAN, The Cambridge Centre for Ageing and Neuroscience, which is a large-scale collaborative research project based at the University of Cambridge. The Cam-CAN project uses epidemiological, behavioural, and neuroimaging data to understand how individuals can best retain cognitive abilities into old age (Cam-CAN, 2011). Access to the dataset is within public domain, and an authorisation form has been submitted to gain access to the dataset for the purposes of this project. The data has appeared several times in the literature (Shafto *et al.*, 2014; Taylor *et al.*, 2017) which means that ethical approval was granted in order to publish those papers.

Clinical MRI data provided by the SharedRoots project at Stellenbosch University will also be used to test the CNN. The dataset is anonymised but still contains biometric data pertaining to the participants such as age and sex. The Shared Roots project has been approved by the Health Research Ethics Committee at Stellenbosch University. Besides, the SharedRoots data will be analysed on the Stellenbosch Cluster, which is where it is stored, to ensure its safety and confidentiality.

Given the data contains sensitive information, precautions to ensure the safety of the data are required. The datasets are to be analysed through a password and security protected supercomputing cluster (SCW, 2019) and Stellenbosch's Cluster. Also, both datasets have received ethical approval documents from their corresponding institutions which will be forwarded to COMSC Ethics before starting the project. Training and Ethics forms are to be completed and sent to COMSC Ethics prior to starting analysis on the data.

Aims & Objectives

The ultimate aim of the project is to develop a Convolutional Neural Network to predict brain age, given raw T1-weighted MRIs as input. This predictive model will detect changes in structural MRIs related to ageing, where changes include the loss of grey-matter, white-matter, and volume in the brain, all common signs of ageing of the brain (Cole *et al.*, 2017). The aims are outlined as follows:

Aims

- Develop a CNN trained on the Cam-CAN dataset to predict brain age based on neuroimaging data
- Apply the model to the Shared Roots dataset which includes Schizophrenia, Parkinson's disease, and HIV data samples to evaluate the brain age delta on neurodegenerative data
- **Desirable aim:** Identify which brain regions play a greater role when predicting brain age

The following objectives suggest how the above aims will be achieved:

Objectives

- Research activation functions and evaluate which model is best suited for the problem e.g., Tanh, ReLu, Leaky ReLu, SoftMax
- Use TensorFlow to develop a Convolutional Neural Network (CNN) to extract features from a raw MRI in 3D
- Train the CNN using the Cam-CAN dataset using cross-validation
- Experiment with a range of CNN architectures to determine which gives the best results
- Use the MVPA toolbox (Treder, 2020) in the last layer of the network to reduce bias in brain age prediction
- Select a method of quantitative evaluation to determine how interpretable and useful the data produced by the model is, and how it increases the transparency of the CNN
- Create data visualisations from the results of the data analysis using matplotlib
- Draw conclusions about the limits of CNN interpretability and whether deep learning models can truly be transparent in the context of clinical MRI predictions

Work Plan

Supervisor Meetings

I have scheduled individual meetings at 11:00 every Thursday with my supervisor, Matthias Treder, up until mid-March. A different supervisor will be taking over from then with presumably weekly meetings as well. These meetings will be held over Microsoft Teams and will be used to discuss progress and any problems encountered.

Weekly Plan

Here is an outline of the key tasks to be completed by the end of each week. This is not a strict plan since the project is an iterative process and I will have to revisit previous tasks in later weeks. Also, there will be unaccounted challenges and issues which could take longer than a week.

- **Week 1:** 01/02 – 07/02
  - Background research: Convolutional Neural Networks and literature on brain age prediction
  - Initial meeting with supervisor to discuss initial plan and ask technical questions
  - Write initial report
- **Week 2:** 08/02 – 14/02
  - Continued background research
  - Finish Convolutional Neural Networks course
  - Decide how many layers, how many filters per layer, activation function and general CNN structure
- **Week 3:** 15/02 – 21/02
  - Continued background research, create a summary to be used in final report
  - Build core of 3D CNN using TensorFlow
- **Week 4:** 22/02 – 28/02
  - Build core of 3D CNN using TensorFlow to predict age and get training and test error
  - Train CNN using Cam-CAN images
- **Week 5:** 01/03 – 07/03
  - Further training and improvements to the CNN
  - Experiment with different CNN architectures (LeNet-5, VGG, ResNet)
- **Week 6:** 08/03 – 14/03
  - Experiment with different CNN architectures and evaluate which one performs best
- **Week 7:** 15/03 – 21/03
  - Test using an unseen portion of the Cam-CAN dataset and/or the Shared Roots data. The CNN should take in unseen MRIs and correctly predict age
  - Evaluate how well it performs using appropriate testing techniques
- **Week 8:** 22/03 – 28/03
  - Evaluate the strengths and weaknesses of the solution
  - Demonstrate with data what it shows
  - Think about what could be improved
- **Easter Recess:** 27/03 – 18/04
  - Catching up if needed

- **Week 9:** 19/04 – 25/04
  - Start writing final report: Background, Approach, Implementation, Evaluation
- **Week 10:** 26/04 – 02/05
  - Continue writing: Results, Introduction, Abstract
- **Week 11:** 03/05 – 09/05
  - Continue writing: Future work, Conclusion, Appendices
- **Week 12:** 10/05 – 14/05
  - Last minute tweaks, testing, debugging, refactoring code
  - Polish report and hand it in

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