List of tasks

Task	Deadline
Investigate data and read literature	4 April
Implement basic EBM, MCMC sampler	17 April
Positional variance matrices and EBM stage histograms for different groups	30 April
Analyse follow-up data, compute prob of remaining CN, MCI over time	7 May
Calculate cut points, sensitivity and specificity	14 May
Temporal diagram hilighting the order in which areas of brain get affected by PCA	21 May
(maybe, if relevant) Comparison of event sequences across left-right hemispheres?	30 May
...	...
Validation of the results, comparison with other methods	20 July
Write the Mres project report	14 August

Aims of the project

Dementia and other related neurodegenerative disorders cost the UK approximatelly £26 billion a year. Developing a clear understanding of how thse disorders operate and progress over time could help us find more effective treatment. This project is investigating the progression of Posterior Cortical Atrophy (PCA), which is an early onset variant of Alzheimer's disease that causes atropy of the posterior part of the cerebral cortex, resulting in disruption of the visual system.

We are planning on modelling PCA using an *event-based model* (EBM), which models the progression of the disease as a sequence of events, where each event corresponds to a biomarker becoming abnormal. Such events could be: (1) a new area of the brain got affected, (2) the patient shows a drop in cognitive test scores. The EBM can calculate the most common progression of the events in the patient cohort and can be used to classify individual patients into the three main groups: cognitively normal, mild cognitive impairment and Alzheimer's disease. The EBM can also be used for longitudinal studies; for instance, it can stage patients after a predefined follow-up period.

The EBM has already been used to study familiar and sporadic Alzheimer's disease and Huntington's disease, and this project aims to apply these techniques in the study of PCA. We will be interested to find the most common event progression or the probability of a patient converting to mild cognitive impairment or Alzheimer's disease over time. If time permits, we can also investigate possible extensions of the EBM, such as allowing for multiple progression sequences (Alex, IPMI).

Summary of progress to date

I have so far experimented with the EBM by trying to reproduce some of the results of A. Young, 2012. We cannot start writing the EBM for the PCA yet, as we are still waiting to receive the dataset from the Dementia Research Center.