Disease Progression Analysis of typical Alzheimers Disease and Posterior Cortical Atrophy

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Progression Of Neurodegenerative Disease

Alzheimer's disease (AD):

- A neurodegenerative disorder that is the usual cause of dementia (60-70% of cases)
- Symptoms: memory loss, problems with language and disorientation, mood swings, loss of motivation

Posterior Cortical Atrophy (PCA):

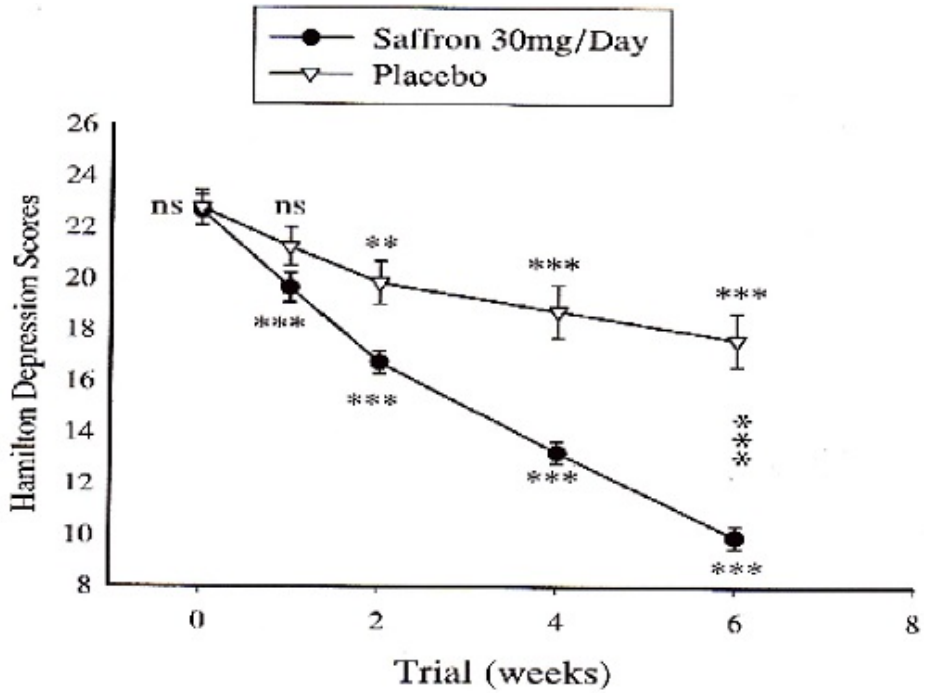
- "Sub-type" of AD that affects the posterior part of the brain
- Symptoms: loss of vision, problems navigating through space, loss of memory only in later stages

Motivation

The development of drugs for AD requires:

- Accurate staging of patients
- A good understanding of the progression of biomarkers
- Taking into account the cohort heterogeneity

Solution: **Disease Progression Models**



Aims

- Develop and improve disease progression models (DPMs)
- Study the progression of typical AD and PCA
- Evaluate the performance of DPMs

Overview

1. **PCA vs tAD Analysis**
2. Performance Evaluation
3. Voxelwise Disease Progression Model (VDPM)

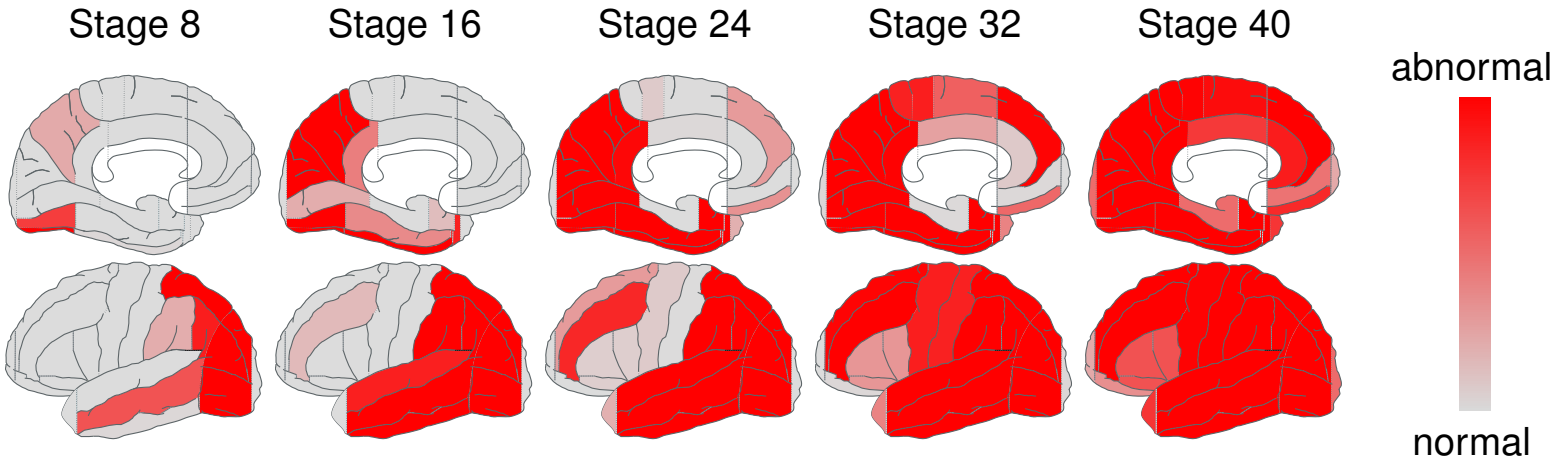
Clinical questions. We want to find differences in timing and rates of atrophy:

- across different brain regions
- in PCA compared to AD

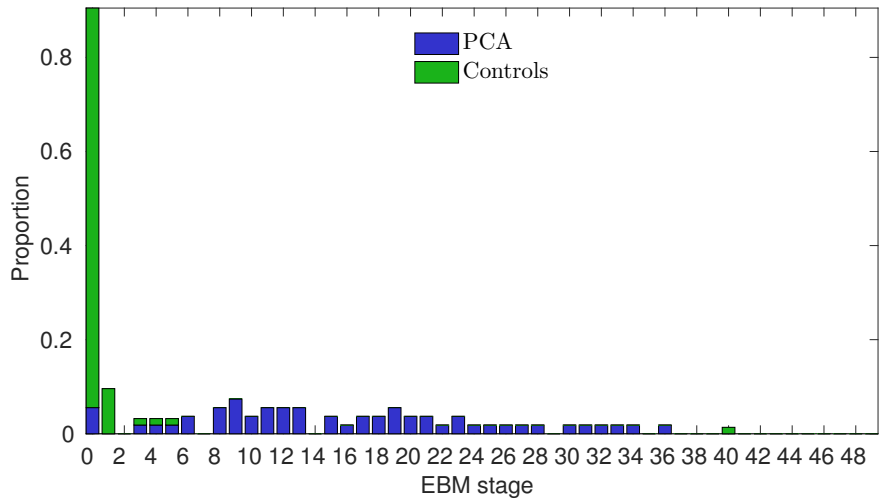
Methods:

- Event-Based Model (EBM)
- Differential Equation Model (DEM)

EBM - Results in Posterior Cortical Atrophy

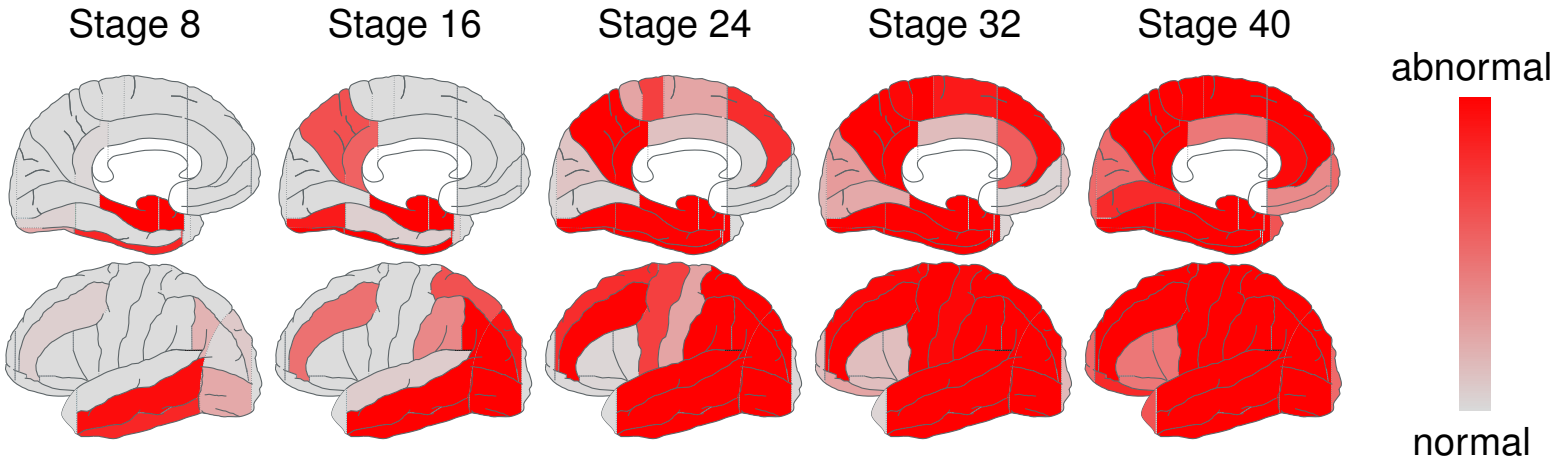


(a) Progression of brain volume loss

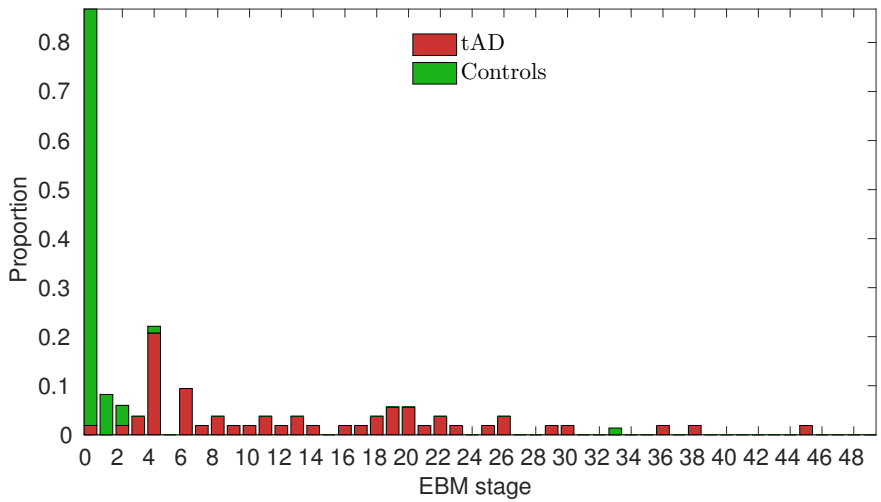


(b) Subject staging

EBM - Results in typical AD

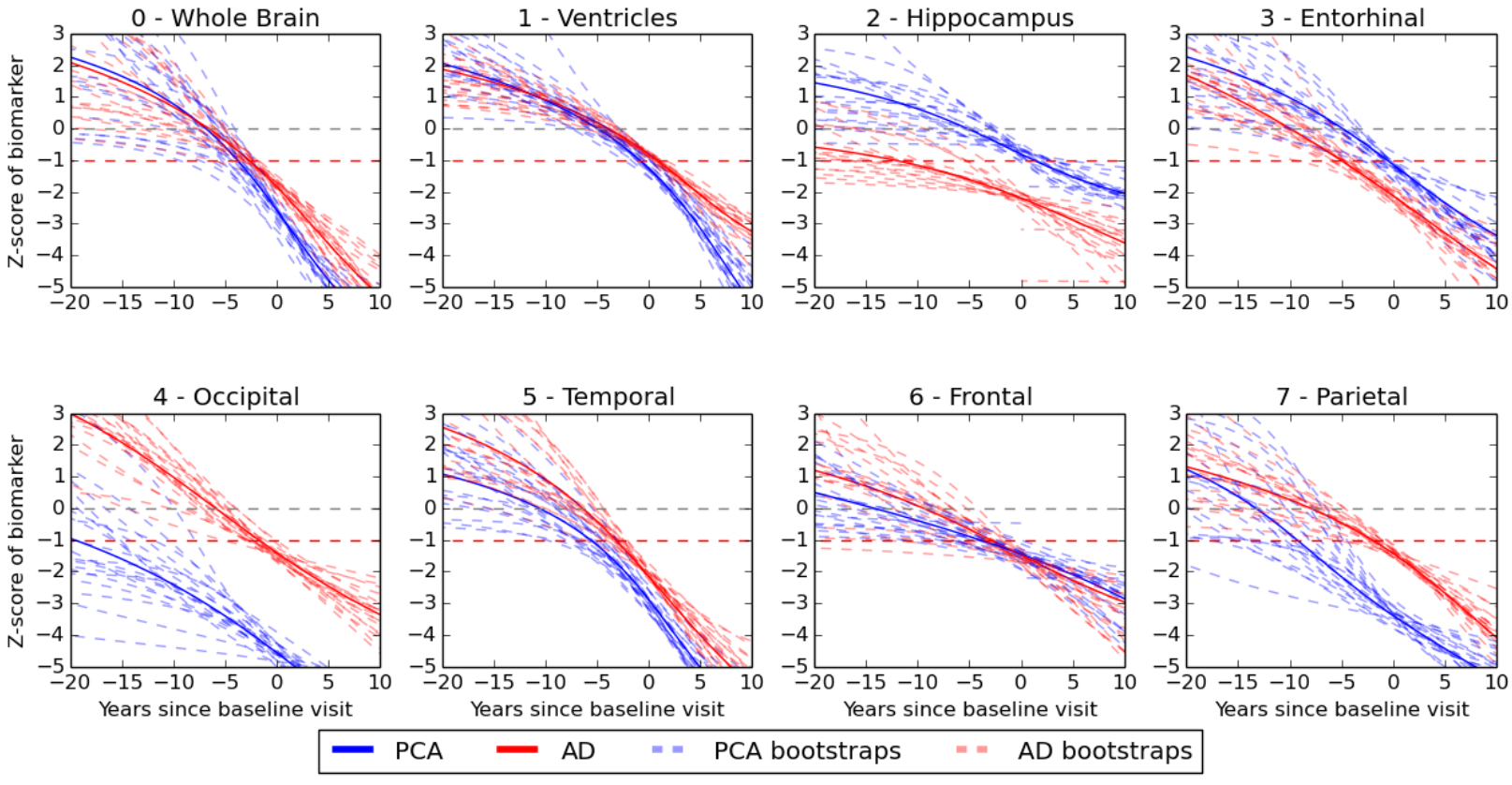


(a) Progression of brain volume loss



(b) Subject staging

DEM - PCA vs tAD progression across ROIs



Conclusion:

- In tAD, the hippocampus and entorhinal areas become abnormal earlier
- In PCA, the occipital and parietal regions becomes abnormal earlier

Overview

1. PCA vs tAD Analysis
2. **Performance Evaluation**
3. Voxelwise Disease Progression Model (VDPM)

Performance Evaluation

Aim

Evaluate the performance of:

- different disease progression models
- different fitting procedures

Methods

- Implemented improved fitting procedures for EBM (2 methods) and DEM (1 method)
- Tested if the improved fitting procedures perform better
- Performed the evaluation on two datasets: ADNI and DRC

Performance Evaluation - Results

Model	Staging Consistency		Time-lapse	
	Hard	Soft	Hard	Soft
EBM - Standard	0.91 ± 0.16	0.71 ± 0.07	-	-
EBM - Sampling	0.96 ± 0.07	0.76 ± 0.10	-	-
EBM - EM	0.99 ± 0.01	0.72 ± 0.07	-	-
DEM - Standard	0.87 ± 0.10	0.88 ± 0.08	0.72 ± 0.91	0.67 ± 0.92
DEM - Optimised	0.87 ± 0.10	0.88 ± 0.08	0.74 ± 0.92	0.69 ± 0.92

Table : tAD subjects from DRC cohort.

Conclusion: Improved methods showed better or equal performance compared to standard methods.

Overview

1. PCA vs tAD Analysis
2. Performance Evaluation
3. **Voxelwise Disease Progression Model (VDPM)**

Voxelwise Disease Progression Model (VDPM)

Motivation:

- Estimate a fine-grained spatial distribution of atrophy
  - without a-priori defined ROIs

Method:

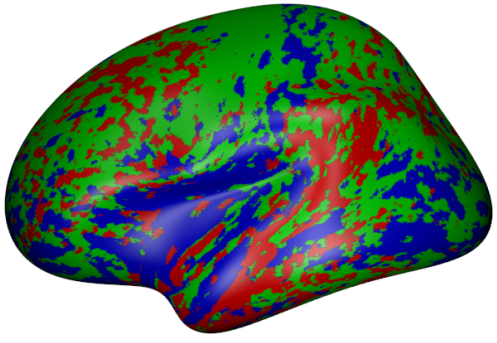
- New model that groups vertices into clusters and stages subjects
- Clusters contain vertices with similar biomarker evolution
- Fitting using Generalised Expectation-Maximisation

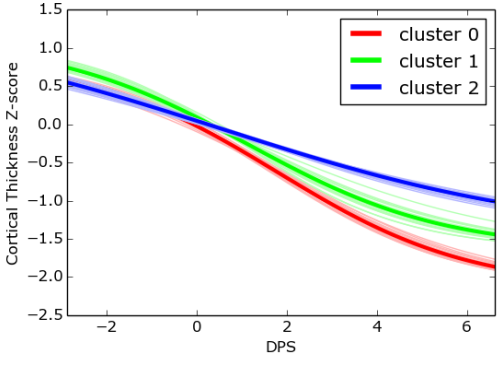
VDPM Results - ADNI and DRC cohorts

rapid atrophy slow atrophy

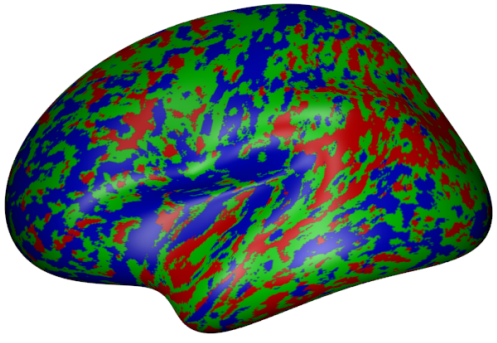
cluster 0 cluster 1 cluster 2

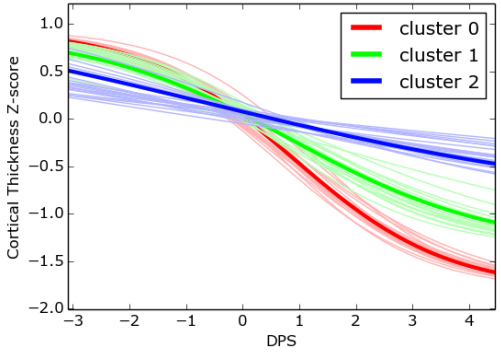
tAD - ADNI



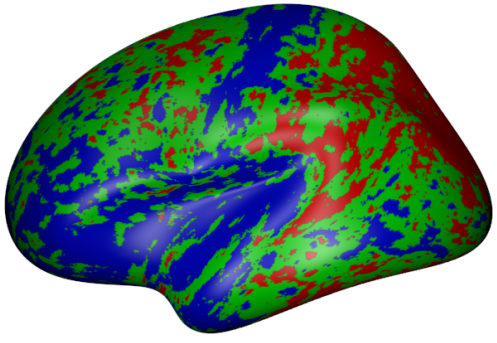


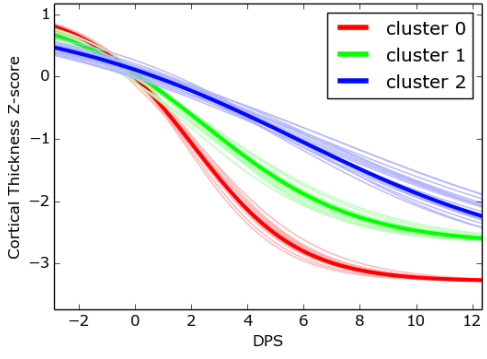
tAD - DRC dataset





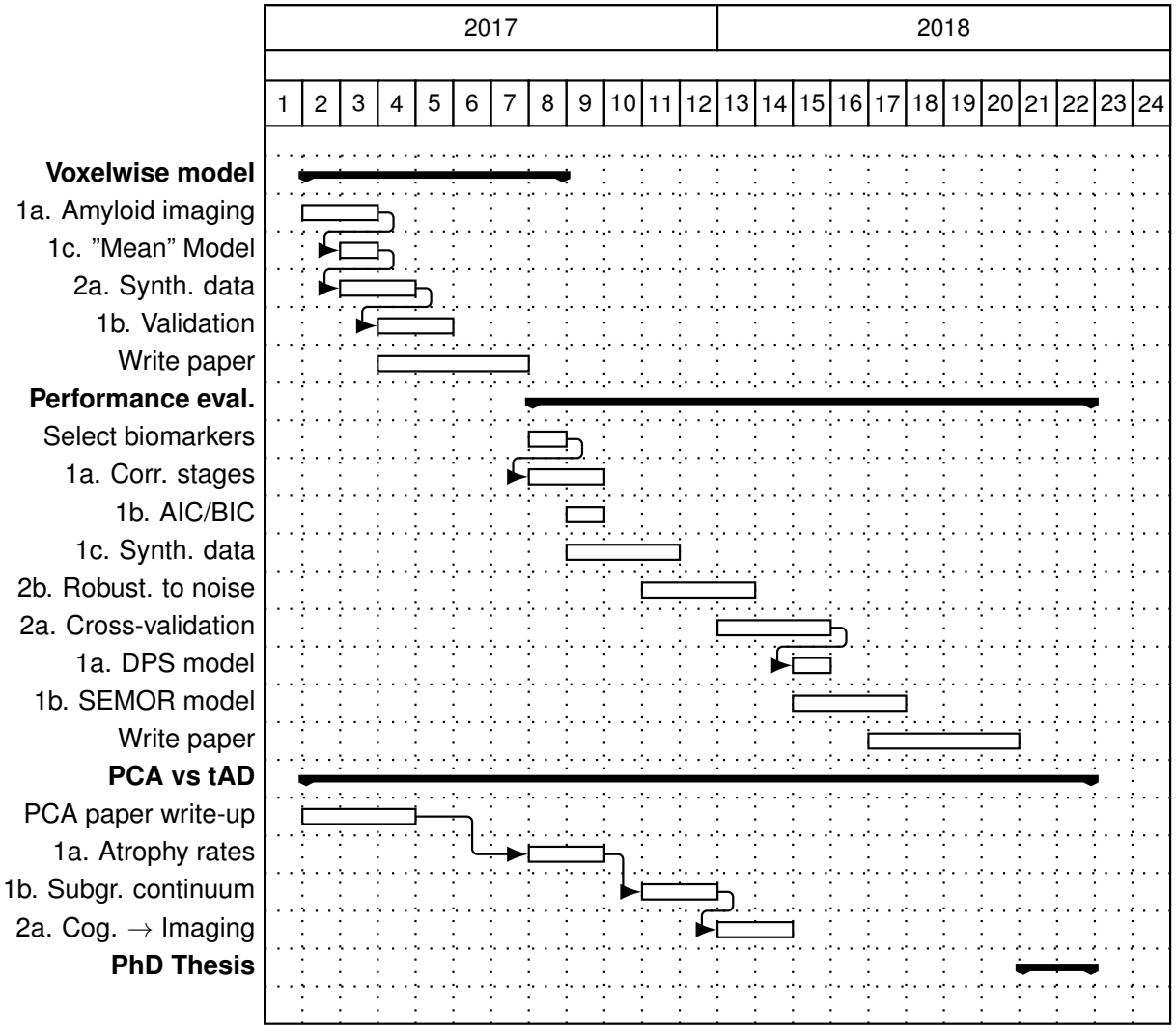
PCA - DRC dataset





Conclusion: We can see a fine-grained spatial distribution of atrophy.

Future Work Plan



Acknowledgements

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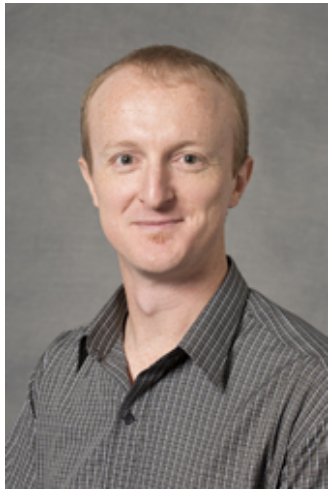
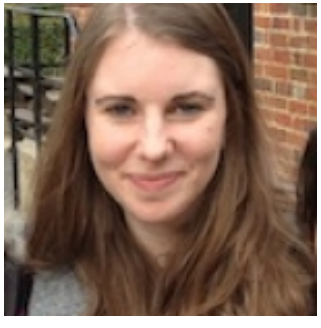


Alexandra Young



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