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DIVE: A spatiotemporal progression model of brain pathology in neurodegenerative disorders

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ABSTRACT

Current models of progression in neurodegenerative diseases use neuroimaging measures that are averaged across pre-defined regions of interest (ROIs). Such models are unable to recover fine details of atrophy patterns; they tend to impose an assumption of strong spatial correlation within each ROI and no correlation among ROIs. Such assumptions may be violated by the influence of underlying brain network connectivity on pathology propagation – a strong hypothesis e.g. in Alzheimer's Disease. Here we present DIVE: **D**ata-driven **I**nference of **V**ertexwise **E**volution. DIVE is an image-based disease progression model with single-vertex resolution, designed to reconstruct long-term patterns of brain pathology from short-term longitudinal data sets. DIVE clusters vertex-wise (i.e. point-wise) biomarker measurements on the cortical surface that have similar temporal dynamics across a patient population, and concurrently estimates an average trajectory of vertex measurements in each cluster. DIVE uniquely outputs a parcellation of the cortex into areas with common progression patterns, leading to a new signature for individual diseases. DIVE further estimates the disease stage and progression speed for every visit of every subject, potentially enhancing stratification for clinical trials or management. On simulated data, DIVE can recover ground truth clusters and their underlying trajectory, provided the average trajectories are sufficiently different between clusters. We demonstrate DIVE on data from two cohorts: the Alzheimer's Disease Neuroimaging Initiative (ADNI) and the Dementia Research Centre (DRC), UK. The DRC cohort contains patients with Posterior Cortical Atrophy (PCA) as well as typical Alzheimer's disease (tAD). DIVE finds similar spatial patterns of atrophy for tAD subjects in the two independent datasets (ADNI and DRC), and further reveals distinct patterns of pathology in different diseases (tAD vs PCA) and for distinct types of biomarker data – cortical thickness from Magnetic Resonance Imaging (MRI) vs amyloid load from Positron Emission Tomography (PET). We demonstrate that DIVE stages have potential clinical relevance, despite being based only on imaging data, by showing that the stages correlate with cognitive test scores. Finally, DIVE can be used to estimate a fine-grained spatial distribution of pathology in the brain using any kind of voxelwise or vertexwise measures including Jacobian compression maps, fractional anisotropy (FA) maps from diffusion tensor imaging (DTI) or other PET measures.

1. Introduction

Many biomarkers exist that can be used to track the severity of neurodegenerative diseases such as Alzheimer's disease (AD). Clinical function can be measured using cognitive assessments performed by an expert clinician and brain atrophy can be measured using Magnetic Resonance Imaging (MRI). Other measures include molecular markers such as aggregation of misfolded amyloid-beta or tau measured using Positron Emission Tomography (PET), and measures of white-matter degradation such as fractional anisotropy (FA) from Diffusion Tensor Imaging (DTI). The evolution of these biomarkers across the disease time-course creates a unique signature of the disease that can be used to stage

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