small world property showed main effects of diagnosis and clinical progression, which is suggestive of a linear trend (Figure 1). Cox analyses indicated that lower values of 5 grey matter network parameters were related to clinical progression: degree (HR = 1.48; 95%CI = 1.09-2.02), connectivity density (HR = 1.49; 95%CI = 1.09-1.81), clustering (HR = 2.92; 95%CI = 1.27–6.69; Figure 2), normalized clustering (HR = 1.47; 95%CI = 1.13-1.91), and small world value (HR = 1.45; 95%CI = 1.13–1.87). No interaction effects of baseline diagnosis and network properties on time to dementia onset were found (all p_{ia} >.05). **Conclusions:** In non-dementia phases of AD, grey matter networks disruptions suggestive of a change towards a more random network organization were associated with time to clinical progression. Our findings suggest that connectivity based markers have prognostic value in amyloid positive individuals.

P1-285 LONGITUDINAL CEREBELLAR CHANGES IN MILD COGNITIVE IMPAIRMENT AND ALZHEIMER'S DISEASE

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Background: While, the acceleration in age-related cerebral atrophy has been well documented in Alzheimer's disease (AD), the cerebellar contributions in AD pathology have considered less likely and have not been as thoroughly investigated as the cerebrum. This study investigated cerebellar volume and longitudinal volume changes using FreeSurfer volumetry and voxel-based morphometry in cognitively normal and impaired groups including mild cognitive impairment (MCI). **Methods:** Multiple linear regressions was used for cross-sectional comparison of the cerebellar volume in 818 ADNI1 participants (CN= 229, MCI=398, AD=191) with screening magnetic resonance imaging, and all subjects with 2 or more follow up scans (N=758) were included for longitudinal evaluation of the cerebellar volume changes using linear mixed effects model. Participants were categorized into different diagnostic groups regarding to their diagnosis at the first and last scans and pair-wised comparison analyses applied. **Results:** Cross sectional analysis demonstrated that cerebellar volume was significantly different between cognitively normal and AD but there were no differences between normal and MCI and MCI and AD. Similarly atrophy rates were slightly different between stable normal and AD groups, normal and MCI converted to AD groups and also stable MCI and MCI converted to AD groups in longitudinal analysis. Volume changes were not different between normal and stable MCI and stable MCI and AD. **Conclusions:** The evidence indicating that cerebellar contributions in AD pathology is relatively small and mostly happen at the late stage of the disease when it is clinically well-developed. Additional work needs to further elucidate the role of biological factors in protecting the cerebellum against the shrinkage.

P1-286 MANIFOLD-VALUED STATISTICAL MODELS FOR LONGITUDINAL MORPHOMETRIC ANALYSIS IN PRECLINICAL ALZHEIMER'S DISEASE

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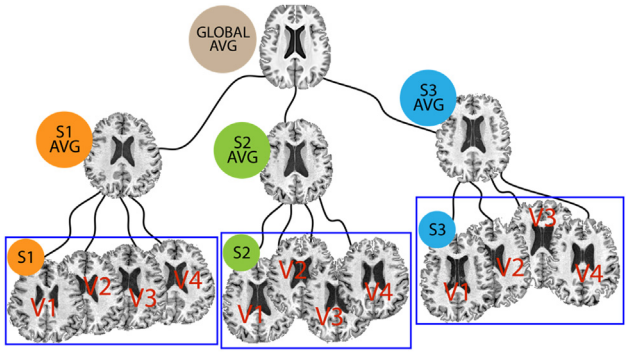
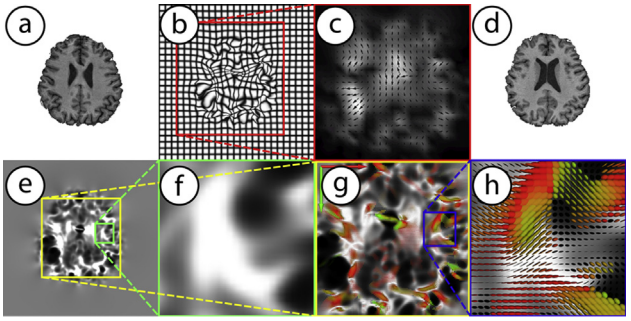
Background: The ability to quantitatively characterize incipient Alzheimer's disease (AD) pathology in its preclinical stage is a critical step for early interventions involving disease modifying therapy and for designing efficient clinical trials to test therapy efficacy. In this project, we propose statistical image analyses for identifying the relationships of morphometric changes in this early stage with direct indicators of AD pathology (such as amyloid deposition) and various risk factors such as family history in late midlife adults who are cognitively healthy. Current state-of-the-art statistical hypothesis testing methods use the so-called *Jacobian determinant* (JD) of the morphometric deformations as the outcome measure. JD captures the volumetric brain changes but during preclinical stages of AD the changes in the brain might not be reflected at the volumetric level. **Methods:** We introduce a new framework that extracts Cauchy deformation tensors (CDT) from the morphometric deformations and performs hypothesis testing. Our algorithms that allow performing multivariate general linear model (MGLM) directly on the manifold-valued representations of morphometric change and consequently yield high sensitivity in picking up real but statistically weak patterns of the disease process. Fig 1. shows our unbiased estimation of the global coordinate system for the longitudinally acquired imaging data. Fig. 2 shows deformation/warp fields of JDs and Cauchy deformation tensors (CDTs). Using a longitudinal dataset of 243 T1-weighted images from Wisconsin



Unbiased estimation of the global coordinate system for the longitudinally acquired imaging data. Visits V1-V4 are averaged first which are then used to estimate the global average.



An example panel of data generated in morphometric studies. (a) The moving brain image. (b) Warped grid to move (a) to (d). (c) Vector field of local deformations. (e, f) det|J| field. (g, h) CDTs ($\sqrt{JJ^T}$). Among the different features of brain morphology that can be analyzed, CDTs are the focus of this project.