Manifold-valued statistical models for longitudinal morphometic analysis in preclinical Alzheimers disease (AD)

https://neurodegenerationresearch.eu/survey/manifold-valued-statistical-models-for-longitudinal-morphometic-analysis-in-preclinical-alzheimers-disease-ad/

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USA

Title of project or programme

Manifold-valued statistical models for longitudinal morphometic analysis in preclinical Alzheimers disease (AD)

Source of funding information

NIH (NIA)

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€ 912,467.89

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30/09/2016

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1

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Statistical Models, Alzheimer disease prevention, Alzheimer's Disease, Adult Children, pre-clinical

Research Abstract
Project Summary 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. This project focuses on deriving statistical image analysis methods for identifying the relationship 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. The proposed analysis will be conducted on the largest preclinical AD cohort assembled to date and help elucidate how clinical-cognitive-imaging AD phenotypes emerge in asymptomatic individuals at risk for AD. The core of our analyses is a set of algorithms that allow operating directly on powerful “manifold-valued” representations of morphometric change and consequently yield high sensitivity in picking up real but statistically weak multi-modal patterns of the disease process. Hypothesis: 1) Detecting precise associations between morphometric changes in preclinical AD subjects with amyloid burden and various risk factors is possible using new algorithms that work directly with representations of the Jacobians of the deformation fields derived from longitudinal imaging data. 2) Conducting such analyses on a large multi-site cohort of asymptomatic at-risk preclinical AD individuals with identified AD pathology will a) reveal important insights into early disease processes when dementia is 15+ years away, b) provide preclinical AD biomarkers and c) provide frameworks for predicting clinical endpoints at the level of individual subjects. Specific Aims: 1) To develop new algorithms for performing statistical analysis of manifold representations of morphometric changes concurrently with multiple covariates representing risk factors, AD pathology markers, and clinical/cognitive measures. 2) Conducting an end-to-end analysis of two independent preclinical AD cohorts to identify the relationship of morphometric changes with various predictors as well as test/retest validation across sites. 3) Analyzing the largest preclinical AD cohort to date for characterizing the relationship of the entire spectrum of predictors to clinical endpoints for late midlife individuals. 4) Providing industry- strength open-source software implementing the full suite of models, integrated with existing software toolboxes, for deployments on a workstation, a high throughput cluster or the cloud. Significance: This project will have a significant impact across three distinct areas of brain imaging research: 1) characterization of how clinical-cognitive-imaging AD phenotypes emerge in asymptomatic individuals in the earliest stages of AD, 2) rigorous algorithms for morphometric change analysis in neuroimaging and neuroscience, 3) open-source end-to-end implementations of the algorithms for use within the community.

Lay Summary

PUBLIC HEALTH RELEVANCE This project will develop novel statistical image analysis methods to characterize complex morphological brain changes in healthy individuals who are at risk of Alzheimer’s disease (AD) and also have some evidence of AD related pathology. Studying and quantifying the evolution of early disease processes in late midlife adults (who are cognitively healthy) on the largest “preclinical” AD cohorts assembled to date will yield frameworks that tie such disease patterns to precise clinical endpoints, such as cognitive decline. These preclinical AD biomarkers have direct applications in a) design of clinical trials for new therapies and b) eventual translation to clinical practice.

Further information available at:

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Investments > €500k

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United States of America

Diseases:
Alzheimer's disease & other dementias

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N/A

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