Understanding, Preventing, Diagnosing, and Treating Alzheimer's Disease: A Multidimensional Alzheimer's Disease Brain Atlas

This project developed a digital atlas of Alzheimer's disease using a framework to correlate disease observations from diverse images in a single probabilistic brain model. The research led to landmark papers and novel methods to characterize and track Alzheimer's disease that are used at imaging centers nationally and overseas.

Lead Agency: National Library of Medicine (NLM), National Institutes of Health (NIH)

Agency Mission:

The mission of NLM is to acquire, organize, disseminate, and preserve the biomedical knowledge of the world for the benefit of the public health. Toward this mission, NLM offers extramural grants for research in biomedical informatics and information sciences, bioinformatics and public health informatics, and supports informatics research training at twenty universities.

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Partner Agencies: National Institute on Aging (NIA), National Institutes of Health (NIH)

General Description:

This project created an atlas of Alzheimer's disease by developing a framework to correlate disease-specific observations from different types of images (such as MRI scans, PET scans, and frozen sections of brain tissue) into a probabilistic brain model presented as a digital atlas. The developed tool set and product are applicable not only to the basic and clinical science of Alzheimer's disease, but to the general problem of mapping the structure and function of any dynamic process in health or disease in whole populations of subjects. This work led to hundreds of publications on new measures track to Alzheimer's disease progression and novel methods for creating digital image atlases. The work combines data from post mortem tissue with images from the various modalities to create a probabilistic model of the brain that provides which regions are most likely to be affected by Alzheimer's. This in turn allows a scientist to compare new images to the atlas and assess the probability that what they are comparing has the disease. The project also developed 4D visualization tools that incorporate spatial and temporal data into profiling how the brain regions degenerate with Alzheimers. The researchers published landmark papers, now very highly cited, in 3 areas: (1) the first time lapse maps of the trajectory of Alzheimer's disease in the living brain; (2) the first reports tracking the spread of plaque and

tangle pathology in the living brain; and (3) registration and analysis of unique brain tissue scans of Alzheimer's disease, which they incorporated into the probabilistic brain atlas. This body of work is now widely cited in the Alzheimer's field. Their methods for tracking Alzheimer's disease are now used at imaging centers nationally and overseas.

Excellence: What makes this project exceptional?

In developing a brain atlas of Alzheimer's disease, the researchers developed the first time lapse maps of the trajectory of Alzheimer's disease in the living brain; published the first reports tracking the spread of plaque and tangle pathology in the living brain; and perfected methods of registration and analysis of unique brain tissue scans into a probabilistic brain model. Their methods for tracking Alzheimer's disease are now used at imaging centers nationally and overseas.

Significance: How is this research relevant to older persons, populations and/or an aging society?

Alzheimer's disease looms as the greatest threat to public health in the first half of the 21st century. Dementia doubles in frequency every five years after age 60, afflicting 1 percent of those aged 60-64 but rising to 30-40 percent of those 85 years or older. The marked growth in the elderly population and the dramatic rise in the frequency of dementia are warnings of an approaching socioeconomic disaster with no cure. The annual cost (direct and indirect) of Alzheimer's disease in the United States alone is over $113 billion.

Effectiveness: What is the impact and/or application of this research to older persons?

This tool set and product are highly applicable to the basic and clinical science of Alzheimer's disease, which remains a significant public health threat for older persons. Future large-scale studies of neuroanatomy in Alzheimer's disease will greatly benefit from this new atlas-based framework for analysis. The time savings for an automated assessment of multiple brain regions over manual brain region delineation methods are enormous.

Innovativeness: Why is this research exciting or newsworthy?

The manual generation of brain region information for the 20 datasets used to construct the probabilistic atlas took over 3000 man-hours to generate. Using the tools and techniques developed in this project, a researcher now needs roughly 15 hours of processing time and 1 hour of visualization of registration accuracy to achieve similar results. Thus, this automated assessment allows a profound time savings. The computational atlas imaging tool accommodates growth in its population data. The population distribution data is made available to the users of this assessment method contingent upon their sharing of their data with other users, which is now the goal of the Alzheimer's Disease Neuroimaging Initiative (ADNI). Through open sharing of similar assessment tools and longitudinal populations, researchers achieve sufficient statistical power to evaluate individual patients against the population. Studies using the ADNI database are now testing the predictive power of this and other assessment tools in identifying incipient Alzheimer's disease within the elderly population.