Modeling Axonal Density and Inflammation-Associated Cellularity in Alzheimer’s Disease Using Hybrid Diffusion Imaging

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USA

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Modeling Axonal Density and Inflammation-Associated Cellularity in Alzheimer’s Disease Using Hybrid Diffusion Imaging

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NIH (NIA)

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1

The project/programme is most relevant to:

Alzheimer's disease & other dementias

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Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Clinical Research...

Clinical Research - Extramural... Dementia... Diagnostic Radiology... Neurodegenerative... Neurosciences... Prevention

Research Abstract

Project Abstract Alzheimer’s disease (AD) affects as many as 5 million individuals over the age of 65 in the United States (US) and 35 million worldwide. Because of the aging population, the prevalence of AD will disproportionately increase in future years if no effective early interventions are developed. Converging evidence suggests that the pathophysiologic processes in the brains of AD patients begin decades before symptoms occur. The long preclinical phase of AD provides a valuable window for early intervention with disease-modifying therapy, if we are able to understand the underlying mechanisms of AD by identifying reliable biomarkers. Diffusion MRI (dMRI) probes microstructures of the human brain by measuring water diffusion properties at the cellular level in vivo and non-invasively, which is especially suitable for preclinical screening and monitoring disease progression for AD. Microstructural features with links to specific biologic targets, e.g., axons, glia, or extracellular substrates may provide direct insight into the pathophysiologic changes underlying neurodegenerative disorders. In theory, diffusion MRI provides significant advances for objectively detecting and characterizing the mechanisms of brain changes in AD. Current approaches using diffusion tensor imaging (DTI), however, have not achieved this potential. A very recent advance in the use of dMRI to image the human brain is the development of a method to reflect axonal density and volume fraction of glial cells (cellularity) among other microstructural features. These biologic specific diffusion metrics can be obtained by parametric analysis of the diffusion data via diffusion compartment modeling. We will use the hybrid diffusion imaging (HYDI) developed by the PI to acquire diffusion data with at least five diffusion-weighting b-value shells to sensitize diffusion compartments (e.g., axons, glia, and extracellular substrates) with different diffusivities. A novel feature of HYDI is its versatility for various diffusion model analyses and computational approaches. In the proposed research, we will use two diffusion modeling approaches: (1) neurite orientation dispersion and density imaging (NODDI) to extract the diffusion metric for axonal density, and (2) diffusion basis spectrum imaging (DBSI) to extract the cellularity of glial cells reflecting inflammatory processes. The goals of the proposed research are to determine the sensitivity (Aim 1), discrimination (Aim 2), and predictive power (Aim 3) of the diffusion metrics of axonal density and inflammation-associated cellularity cross-sectionally (Aims 1 and 2) and longitudinally (Aim 3) in a cohort of healthy control and preclinical (at-risk) older adults, and patients with early mild cognitive impairment (MCI), late MCI, and AD. The success of the proposed research will lead to the development of non-invasive differential diagnostic tools and reveal the micromechanisms of the pathophysiologic changes that occur in the early stages of AD.

Lay Summary

Project Narrative Public Health Relevance Alzheimer’s disease affects as many as 5 million individuals over the age of 65 in the United States and 35 million worldwide. The best treatment is prevention, which requires objective diagnostic tools for early detection. To this end, the proposed research aims to identify novel microstructural imaging biomarkers obtained with magnetic resonance imaging as early differential diagnostic tools.

Further information available at:

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Investments > €500k

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United States of America

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Alzheimer's disease & other dementias

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2016

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