Early-Onset Alzheimers Disease Phenotypes: Neuropsychology and Neural Networks

https://neurodegenerationresearch.eu/survey/early-onset-alzheimers-disease-phenotypes-neuropsychology-and-neural-networks/

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Early-Onset Alzheimers Disease Phenotypes: Neuropsychology and Neural Networks

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1

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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)... Basic Behavioral and Social Science... Behavioral and Social Science... Bioengineering... Brain Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Mental Health... Neurodegenerative... Neurosciences

Research Abstract

? DESCRIPTION (provided by applicant): Unlike the usual late-onset Alzheimer's disease (LOAD), early-onset AD (EOAD), with onset before age 65, includes a high percentage of phenotypic variants. These non-familial, variants (vEOAD) present, not with progressive memory loss, but with language, visuospatial, or other cognitive difficulties. We now understand AD as a disorder that manifests with disturbed cognition reflecting disturbed neural networks. A multivariate analysis of neuropsychological tests, the ""gold standard"" for objectively defining neurocognitive impairments, coupled with structural and functional neuroimaging analysis of connectomes, can identify the neurocognitive-neural network profiles of vEOAD patients, compared to those with typical AD. This knowledge can increase our understanding of the heterogeneity of AD and how it causes disease. Objective. This proposal aims to show that vEOAD comprises its own clinical-neurobiological disorder, or ""type 2 AD"", evident by a specific neurocognitive profile on neuropsychological tests and by specific structural and functional neural network involvement on magnetic resonance imaging (MRI). The neurobiology of Type 2 AD, which is composed of overlapping clinical syndromes that cluster together, challenges the prevailing view of initial ?42-amyloid deposition followed by neurofibrillary tangle (NFT) formation in the entorhinal- hippocampal cortex, and suggests involvement and propagation via alternate neural networks. Methods. This study recruits 60 vEOAD patients, 30 typical amnestic EOAD patients, and 30 typical LOAD patients as well as 60 normal, age-matched controls. In Specific Aim 1, all participants undergo neuropsychological tests and neurological tasks related to potentially affected brain regions. It assesses and corroborates a proposed neuropsychological test profile for the diagnosis and one-year follow-up of Type 2 AD. In Specific Aim 2, the EOAD participants undergo MRI measures of structural and functional neural networks using connectomic analysis of diffusion tensor imaging and resting-state functional MRI. Anticipated Results. This proposal hopes to show that vEOAD constitutes a ""Type 2 AD"". Specific Aim 1 defines the neuropsychological components of Type 2 AD. Specific Aim 2 shows that, compared to typical amnestic EOAD or LOAD, Type 2 AD initially spares entorhinal-hippocampi cortex and the default mode network in favor of alternate frontoparietal networks (e.g., central executive network). Together, these specific aims define the distinct neurocognitive-neural network profile of Type 2 AD compared to typical amnestic AD. Conclusions. By recognizing the underlying neurocognitive-neural network profile of Type 2 AD in relation to typical AD, researchers gain crucial knowledge of the variations in the pathophysiological manifestations and neural propagation of this disease. In addition to information that can help in the diagnosis and management of EOAD, this proposal can stimulate novel research into the reasons for this neurobiological heterogeneity in AD and could potentially lead to interventions based on alternate neurocognitive-neural network profiles.

Lay Summary

PUBLIC HEALTH RELEVANCE: Through investigating the atypical forms of Alzheimer's disease, we can increase our understanding of its underlying mechanisms and how it leads to dysfunction in the brain. This type of scientific understanding is important for the development of treatments and other interventions for this devastating disorder.

Further information available at:

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Investments > €500k

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