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Are some human brains able to resist Alzheimer’s pathology?

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Collaborating centers
University of Pittsburgh and Mayo Clinic

Project description
It is clear from recent clinical-neuropathological correlation studies and from PET amyloid imaging studies that there can be a dissociation between the occurrence of Alzheimer pathology and cognitive impairment. The overall goal in this proposal is aimed at testing one of two competing hypotheses, are some human brains resistant to the insult of Alzheimer’s pathology i.e. beta-amyloid (Abeta plaques and neurofibrillary tangles, or is the Abeta phenotype (oligomeric Abeta vs. fibrilar amyloid plaques) what determines structural damage and impaired cognition in Alzheimer’s disease?

We refer to “mismatches” as cases of Alzheimer’s disease by neuropathological criteria that were tested during life and found to be clinically normal. Although quite uncommon, we believe that these cases may be of importance to understand why some individuals with substantial Alzheimer pathology do not get demented, and may contribute to provide a rational approach to neuroprotective and cognitive sparing therapies in the elderly. We propose to pool resources from 3 Centers, the Massachusetts ADRC, the Pittsburgh ADRC, and the Mayo ADRC, that are each actively studying this problem to take advantage of the larger sample size afforded and to share expertise and technologies uniquely available at each site to accelerate answers to these important questions. We plan to use a combination of quantitative histopathology for standard markers of histopathology with the innovative PIB quantitative studies and the Bioplex assays to extend our understanding of these cases towards biochemical and molecular characterization.

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