NACC Project #2001-03
Neuropathologic Correlates of Nondemented Aging

Principal investigator
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Collaborating centers
Duke University, Mayo Clinic Rochester, Oregon Health Sciences University, University of California San Diego, University of Kentucky, University of Rochester

Project description
Clinicopathologic observations from adult cases with Down Syndrome and from a select few normal elderly individuals suggest that histopathologic Alzheimer's disease (AD) may be present for many years prior to the onset of dementia. The possibility that the lesions of AD may exist for years without causing cognitive symptoms has implications for the diagnosis and especially the therapy and prevention of AD. The extent to which a truly preclinical stage of AD is present in nondemented elderly cannot be resolved at present, however. It also remains unknown whether AD neuropathology may underlie the cognitive impairment or decline that often is ascribed to age alone or to possible “transition” states of mild cognitive impairment (MCI) that lack sufficient dysfunction for the diagnosis of dementia.

This collaborative project is addressing these issues with two specific aims: 1) Determine the relationship of histopathologic AD with age in a sample of nondemented elderly individuals; and 2) Evaluate the cognitive status of the nondemented individuals with histopathological AD in comparison to those without AD.

These aims help test the main hypothesis that histopathologic AD occurs in a substantial percentage of nondemented elderly individuals in the absence of cognitive impairment, thus establishing a preclinical stage of AD. This project capitalizes on an NIA-funded study (Neuropsychological Database Initiative; M. Grundman, PI) that examines cognitive correlates of nondemented aging. Nondemented cases submitted to the NDI from the seven Centers participating in the Grundman project which were examined post-mortem will be re-examined in accordance with a standard neuropathologic protocol to identify and quantitate AD lesions. (Uniform cognitive and neuropathologic procedures were established by a consensus conference of investigators from each of the seven Centers prior to data collection.) The neuropathologic data are being correlated with the presence or absence of MCI and other measures of cognitive decline (already collected as part of NDI). The database developed by this proposal will be available for other collaborative studies and will be used to foster new applications that examine the neuropathologic correlates of nondemented aging.

Contact information
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