Clinical Phenotypes of FTD are Determined by Neuropathologic and Biochemical Features

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Project description
There is a high degree of consensus on the clinical and neuropathologic criteria for the diagnosis of Alzheimer disease (AD), and clinico-pathologic concordance is substantial. In contrast, both the clinical and neuropathologic features of the array of disorders under the rubric “frontotemporal dementia” (FTD) are heterogeneous and clinico-pathologic concordance is less robust. Emerging immuno-histochemical techniques continue to reveal new neuropathologic features associated with FTD, such as tau, ubiquitin, alpha-internexin, and valosin-containing protein cellular inclusions that further serve to distinguish among FTD variants. The proposed project is an initial step in the creation of a consortium for the study of FTD in centers distributed throughout the mid- and southwest US. The goal is to combine resources in the ADCs to apply a common protocol for the prospective clinical and neuropathologic depiction of frontotemporal disorders. Retrospective analysis will also be carried out on the pooled 271 autopsied cases from our centers for the purpose of improving clinico-pathologic accuracy, with an emphasis on language-predominant dementia. The specific aims are to: 1) Refine and standardize a common protocol for unbiased neuropathologic classification that will be applied to all prospective autopsy cases and, in abbreviated format, to all archived cases of FTD; 2) Develop and standardize a common protocol for retrospective chart review of archived cases to identify initial symptoms (language, behavior/executive, memory, other) and other clinical and demographic features, and develop a clinical/neuropsychological protocol for prospective enrollment of future cases; 3) Analyze the relationships between clinical symptoms and selected neuropathologic features in the retrospective sample. It is hypothesized that ubiquitin-positive, tau-negative pathology in the temporal lobe will be a feature common to all cases with aphasia at onset; and 4) Determine the impact of the Neary et al. criteria for the diagnosis of frontotemporal lobar degeneration with regard to clinical utility and diagnostic accuracy. The unbiased comparison of individual clinical and neuropathologic features has not been systematically undertaken to date on a large sample and may help bridge the gap between clinical and neuropathologic diagnosis in these disorders.

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Rev. 10/25/2005