Alzheimer’s disease (AD) is a progressive neurodegenerative illness characterized by a persistent loss of memory and impairment in other cognitive functions. Antemortem diagnosis of this disease is primarily done by exclusion of other causes of dementia, while the postmortem diagnosis is based upon the presence of large numbers of neuritic plaques (NPs) and neurofibrillary tangles (NFTs) in conjunction with a clinical history of dementia (1,2). The classical hallmarks of AD have been extensively investigated and described in the scientific literature. Senile plaques in cerebral grey matter have been described already in 1892 by Block and Marinesco (3) and by Redlich in 1898 (4). Neurofibrillary changes were described by Alzheimer in 1907 (5) and dystrophic neurites have been described by Tomlinson et al in 1970 (6), as twisted processes which are probably identical with the neuropil threads visualized by Braak et al in 1986 (7). The use of NPs and NFTs as the basis for definitive diagnosis has some serious drawbacks: to start with, AD is characterized by neuronal loss in the cortex which is not always followed by concomitant change in densities of NPs and NFTs (8). In addition, these well-accepted markers of AD are also present in brains of aged controls and of patients with other neurological diseases (8–11). Moreover, NPs and NFTs are nonuniformly distributed over various brain regions, and the histopathological diagnosis of AD is mainly qualitative, is time-consuming and demands very experienced people. For the reasons listed above it is desirable to have an assay based on a specific marker of AD which combines reproducibility, rapidity and specificity for the disease.

A monoclonal antibody against AD brain homogenates has been developed (12,13). This antibody, called Alz-50, recognizes a neuronal antigen of 68 kDa (A68) which is expressed in AD and in some Down’s syndrome brains (13–15). However, since some normally occurring brain proteins crossreact with Alz-50 in immunoassays and in western blots (16,17), a biochemical assay has recently been developed which is based upon a combination of the monoclonal Alz-50 and a polyclonal rabbit antibody (PR1) raised against a highly ADAP-enriched brain protein fraction. In
this way the crossreactivity with normal brain components is minimized (18,19). The biochemical assay is thought to be an important contribution to the histopathological diagnosis of AD.

**Diagnosis of AD**

The patients have been clinically diagnosed as ‘probable AD’ according to the NINCDS-ADRDA criteria (20) and they all had a global determination scale (GDS) of 6–7 for severity of dementia (21). The neuropathological diagnosis of ‘changes compatible with AD’ or ‘no pathology’ for controls was performed by the same neuropathologists on formalin-fixed specimens (fixation duration, 1 month) and was based upon the distribution and amount of plaques and tangles in sections stained by the conventional histopathological staining procedures. The individuals carrying out the biochemical assay were blind to the clinical and neuropathological diagnoses.

**Statistical analysis**

Because the measured values of ADAP concentrations are truncated at 0 and 2, non-parametric statistics were chosen to analyze the data (22). The Mann-Whitney test was used to compare the non-AD group with the AD group. The Wilcoxon signed ranks test was used to compare frontal with temporal lobe in the three patient groups.

**RESULTS**

The concentration of Alzheimer’s disease associated protein (ADAP) was measured in postmortem brain tissue samples of inferior temporal or superior frontal cortex from 30 human brains and results were expressed as absorbance units per mg protein. The normal group as well as the non-AD dementia group had essentially low levels of ADAP in both frontal and temporal lobe specimens: normal controls, 0.17±0.06 and 0.33±0.03 absorbance units/mg protein respectively; and non-AD dementia, 0.30±0.06 and 0.58±0.10 absorbance units/mg protein respectively. The AD group had substantial ADAP levels in frontal and temporal lobe specimens: 3.62±0.90 and 7.43±0.72 absorbance units/mg protein respectively.

**CONCLUSIONS**

1. The method described in this paper can reliably measure ADAP, providing a unique biochemical laboratory test for postmortem diagnosis of AD. This assay is rapid and simple to run, the supplies are standardized, the equipment is readily available and sample requirements are low (about 100 mg tissue for homogenization).

   The biochemical Alz-EIA offers a rapid, easily performed and quantitative diagnostic method which may serve as a valuable aid to the clinico-pathological diagnosis of AD.

2. It is apparent from these data that the enzyme-linked immunoassay (Alz-EIA) clearly distinguishes ADAP levels in AD brains from controls and other
neurological diseases. The ADAP levels in the AD group were significantly higher as compared with the non-Alzheimer dementia ($P<0.002$) although the mean age of the NAD group (85.7±2.1 years) was higher than the mean age of the AD patients (75.8±2.0 years).

3. In addition, a regional variation was found between frontal and temporal lobe specimens which agrees with the classical neuropathological findings (23).

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