**Objective:** To determine whether higher brain levels of choline acetyltransferase (ChAT) are associated with improved neuropsychological function in patients with Alzheimer disease (AD).

**Design:** Case series with single-blind post hoc analysis of biopsy specimens.

**Setting:** Urban hospital and medical school.

**Patients:** A consecutive sample of 8 patients with AD undergoing brain biopsy and surgical implantation of intraventricular pumps for administration of potential chemotherapeutic agents.

**Interventions:** Brain biopsy, surgical implantation of intraventricular pumps, and, in 1 patient, ventriculo-peritoneal shunt placement.

**Main Outcome Measures:** All patients underwent neuropsychological testing no more than 2 weeks before surgical biopsy. Levels of ChAT were determined in fresh brain tissue from biopsy samples.

**Results:** Significant positive correlations were found between ChAT levels and 2 neuropsychological test scores, Mini-Mental State Examination and the Logical Memory subtest of the Wechsler Memory Scale.

**Conclusion:** Degeneration of the cholinergic system in vivo correlates with decreasing cognitive function in patients with AD.

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**RESULTS**

Histopathological analysis confirmed the diagnosis of AD in all 8 patients.

Neuropsychological scores are shown in Table 1, and correlations are described in Table 2. Significant positive correlations were found between ChAT levels and 2 neuropsychological test scores (Figure). Patients demonstrating higher Mini-Mental State Examination scores also had higher ChAT levels ($P = .03$). Higher Wechsler Memory Scale Logical Memory scores were also associated with higher ChAT values ($P = .05$).

**COMMENT**

The most striking alteration seen in neurotransmitters in AD occurs in the cholinergic system.10,11 Clinical trials using cholinergic agents have shown promising reduction of the mental impairment seen in AD.15-21 The consistency with which this biochemical disruption is seen in...
AD and its association with mental impairment have led to the general acceptance and refinement of the cholinergic hypothesis of dementia in AD. Indeed, the animal models that have been developed to simulate AD focus on disruption of the cholinergic system.

To date, the human tissue analysis that has verified cholinergic involvement in AD has been performed on post-mortem tissue. As neurotransmitter levels can change rapidly following death, it is likely that postmortem tissue levels are different from those in premorbid brain.

Our study analyzed fresh tissue from biopsy samples. In our patients, lower levels of cortical ChAT were negatively associated with neuropsychological performance. Our results indicate that in patients with biopsy-confirmed AD, there is an in vivo loss in ChAT level that correlates with severity of disease measured by loss of neuropsychological function.

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Table 1. Neuropsychological Assessment Scores*

<table>
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<th>Patient No.</th>
<th>MMSE</th>
<th>GDS</th>
<th>WMS-LM</th>
<th>WMS-LMD</th>
<th>WMS-VRD</th>
<th>BN</th>
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</table>

* MMSE indicates Mini-Mental State Examination; GDS, Global Deterioration Score; WMS-LM, Logical Memory subtest of the Wechsler Memory Scale; WMS-LMD, Logical Memory Delayed subtest of the WMS; WMS-VRD, Visual Reproduction Delayed subtest of the WMS; BN, Boston Naming Test; and ellipses, not done.

Table 2. Correlation of MMSE With Other Neuropsychological Tests*

<table>
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<th>Test</th>
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<td>BN</td>
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<td>.06</td>
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</table>

*Abbreviations are explained in the footnote to Table 1. † Indicates P value of correlation.

REFERENCES