

# The Oldest Alzheimer's Patients: Less Pathology but Similar Impairment

**P**HILADELPHIA—A new study reveals that Alzheimer's disease patients age 85 and older have less neocortical pathology and cholinergic dysfunction than do patients a decade or more younger, even though their scores are essentially identical on neuropsychological measures. "Surprisingly, the oldest old seem to need less pathology to come to the same clinical end point and to look similarly demented," noted lead author Annette R. Merdes, MD, who presented the findings at the annual meeting of the American Academy of Neurology.

Dr. Mendes and her colleagues retrospectively examined data for two groups of patients with mild Alzheimer's disease: 15 whose age of onset was after age 85 (the "oldest old") and 60 patients with age of onset between 69 and 75 (the "elderly"). The two groups were matched on the basis of educational level; patients were excluded if there was evidence of familial Alzheimer's disease. The subjects had undergone comprehensive annual neurological and neuropsychological evaluations and came to autopsy between 1985 and 2000.

Although dementia severity was comparable in the two groups, the investigators found lower levels of neocortical and limbic neuritic plaques in the oldest old: Their mean Braak stage was 4.1,

compared to 5.8 in the elderly. Neocortical synaptic density, estimated using a dot-immunobinding assay for synaptophysin, was similarly decreased in both groups. Moreover, the oldest old had higher neocortical choline acetyltransferase levels and markedly fewer neocortical neurofibrillary tangles compared to the elderly patients, although hippocampal tangle burden did not differ between the two groups.

Apolipoprotein  $\epsilon 4$  allele frequency was lower in the oldest old than in the elderly: 14% of the younger group but none of the older patients were  $\epsilon 4$  homozygous. In addition, the duration of the disease was significantly shorter in the oldest old, reported Dr. Merdes, who is a Visiting Fellow in the Department of Neurosciences at the University of California—San Diego Alzheimer's Disease Research Center.

In general, the findings suggest that the pathological burden does not need to be as high for the oldest old to become clinically demented as it does for a younger person to do so. "It would be very interesting to know the mechanism for this difference," noted Dr. Merdes, adding that she and her colleagues plan to continue their studies in this area.

—Leslie Rosenberg