EDITORIAL

The Scintigraphic Appearance of Alzheimer's Disease: A Prospective Study Using Technetium-99m-HMPAO SPECT

Editor's Note: See corresponding article by Holman et al. on pages 181–185.

Dr. Holman and his colleagues have performed an extensive study of the relationship between the scintigraphic patterns of patients with memory and cognitive impairments and clinical diagnosis. Using ^{99m}Tc-HMPAO SPECT, 132 consecutive patients with cognitive or memory impairments underwent SPECT scans. They were subsequently followed for approximately 10 mo, during which a clinical diagnosis of Alzheimer's disease was made using NINCDS criteria for probable Alzheimer's disease. In this manner, it was possible to compare the scintigraphic patterns on the SPECT scan with the clinical diagnoses of these patients.

SPECT data were classified into a number of perfusion patterns, specifically, normal, bilateral posterior temporal and/or parietal cortex defects, bilateral posterior temporal and/or parietal cortex defects with additional defects, unilateral posterior temporal and/or parietal cortex defects with or without additional defects, frontal cortex defects alone, other large (>1 cm) defects, or multiple small (≤1 cm) cortical defects. Of the 113 patients who completed the study, 15 were given a diagnosis of probable Alzheimer's disease. Abnormal perfusion patterns of the bilateral temporoparietal type were associated with Alzheimer's disease in 82% of the cases. Seventy-seven percent of bilateral temporoparietal defects with additional defects were associated with a clinical diagnosis of Alzheimer's disease. Other defects were far less commonly encountered in the patients with a diagnosis of Alzheimer's disease. Thus, these results confirm the impression, previously established, that bilateral temporoparietal defects are commonly confronted in Alzheimer's disease.

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The key question surrounding the ultimate clinical utility of this study is the degree to which recognizable scintigraphic patterns using SPECT scanning are predictive of Alzheimer's disease. This issue can be rephrased in a somewhat more sophisticated manner by asking what was the ultimate validator of diagnosis. Holman and colleagues have chosen to validate SPECT patterns against the clinical judgment of senior physicians who used NINCDS criteria, noting that these criteria are in fact autopsy-validated in 90% of cases. Others have reported the accuracy of NINCDS criteria as ascertained by autopsy confirmation as approximately 80% (*1*). In either circumstance, the diagnostic accuracy of NINCDS criteria for Alzheimer's disease is rather high. The utility of additional diagnostic studies must be assessed against this capacity to augment diagnostic accuracy. Demonstration of enhancement of diagnostic accuracy as a consequence of scintigraphic patterns on SPECT would require validation against an autopsy-confirmed sample. Obviously, such an approach will take considerably longer than the 10-mo follow-up in the Holman et al. investigation. However, this study, with its prospective design, certainly offers the basis for autopsy confirmation if this initial cohort is followed over the ensuing years. One can only hope that resources will be available to allow such a prospective longitudinal study to occur, as its value to clinicians is potentially immense.

There are alternative ways to validate scintigraphic patterns of perfusion in Alzheimer's patients. The hallmark of Alzheimer's disease is progression. With clear cut progression, and the use of NINCDS diagnostic criteria, a relatively accurate diagnosis of Alzheimer's disease can be made. However, these stringent criteria generally require at least moderate disease and are often inconclusive in patients with less severe symptoms. The early case of Alzheimer's disease remains the most problematic to diagnose. This group constitutes a cohort of patients the clinician is most prone to misdiagnose or defer diagnosis. As experimental therapeutic agents designed to slow the progression of Alzheimer's disease are brought to the clinic, accurate early diagnosis will become even more essential. It is perhaps in these patients that scintigraphic studies may eventually prove to have their greatest value. Thus, subsequent research might focus on the predictive validity of scintigraphic patterns of perfusion with ^{99m}Tc-HMPAO or related compounds in patients with the very earliest possible symptoms of Alzheimer's disease to determine if their subsequent clinical course and eventual meeting on NINCDS criteria for Alzheimer's disease was predicted by SPECT at the time of their initial presentation with early disease. Extending such an analysis even further to first degree relatives of Alzheimer's patients over age 65, who may have a high risk for Alzheimer's disease, is yet another important population requiring study.

Finally, a note regarding another real diagnostic dilemma in the assessment of dementia, the patient with multi-infarct dementia. Clinical criteria for multi-infarct dementia are not accurate (*2,3*). Up to 50% of patients given the clinical diagnosis of multi-infarct dementia are found at autopsy to have either Alzheimer's disease, or Alzheimer's disease and multi-infarct dementia. It seems very unlikely that, using current clinical criteria, it will be possible to validate any scintigraphic pattern to be associated with multi-infarct dementia. Rather, it will be essential that such studies use autopsy-validated diagnoses to indicate that any scintigraphic pattern is actually associated with multi-infarct dementia.

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