Summary

Alzheimer’s disease is associated with reductions of regional cerebral blood flow and metabolism. Since the development of the $^{133}$Xe inhalation technique for tomographic measurements of regional cerebral blood flow, single photon emission computer tomography (SPECT) of the brain has played an important role in the study of dementia disorders. Recently, hexamethyl-propylene-amine-oxime ($d,l$-HMPAO) for labeling with $^{99m}$Tc was developed as a tracer for regional blood flow distribution studies by SPECT.

In an ongoing study of $[^{99m}$Tc]$\text{HMPAO}$ SPECT in dementia and normal aging, 18 patients fulfilled the clinical criteria for “probable Alzheimer’s disease.” In 17 patients the regional cerebral blood flow pattern was rated as abnormal by visual inspection. In eight patients regional cerebral blood flow was reduced primarily in posterior temporoparietal regions. In four patients regional cerebral blood flow was reduced primarily in the frontal lobe, although often with some temporal lobe involvement, and in five patients frontal and posterior areas were equally affected. These changes were not associated with any focal parenchymal changes in the X-ray computer tomography (CT) scans. The diverse localizations of regional cerebral blood flow reductions were in good agreement with the clinical symptoms, and may reflect different subgroups or stages of Alzheimer’s disease.

Brain imaging with SPECT provides functional information correlative to neuropsychological data and may be helpful in evaluating treatment effects and prognosis. However, only studies with repeated evaluations of patients until neuropathological confirmation of the diagnosis will reveal the exact diagnostic and prognostic value of SPECT in Alzheimer’s disease.

Introduction

Alzheimer’s disease is associated with reductions of regional cerebral blood flow and metabolism. Tomographic measurements of regional cerebral blood flow with single photon emission computer tomography (SPECT) were first made possible by the $^{133}$Xe inhalation technique (Celsis et al. 1981; Stokely et al. 1980).
This method facilitates repetitive quantitative studies and, hence, vasoactive stress tests, which in some patients may contribute important information for the differential diagnosis of dementia. However, the technique requires special SPECT equipment and is associated with some drawbacks, such as artifacts due to the high concentration of $^{133}$Xe in the nasal airways and a low resolution, which to some extent limit its use in the regional mapping of dementia disorders. New $^{99m}$Tc-labeled tracers, which are trapped in the brain as a function of the blood flow, have been designed for SPECT. Hexamethyl-propylene-amine-oxime ($d,l$-HMPAO) for labeling with $^{99m}$Tc is one such new radiopharmaceutical introduced as a tracer for cerebral blood flow (Neirinckx et al. 1987; Andersen et al. 1988). In the brain it is rapidly converted to a hydrophilic form which is retained for several hours. The steady-state distribution in the brain is almost proportional to regional cerebral blood flow. Therefore, imaging of tracer uptake in the brain may be performed using a conventional rotating gamma camera, and with a dedicated SPECT camera a very high resolution is attained. Thus, although no follow-up studies have been performed, $[^{99m}$Tc$]$HMPAO SPECT could play a widespread and important role in the routine differential diagnosis of dementia, and in the subgrouping and prognostic rating of patients with Alzheimer’s disease.

This paper discusses the use of SPECT as a functional neuroimaging technique in relation to dementia of the Alzheimer type. A preliminary report on patterns of regional cerebral blood flow abnormalities in a group of 18 patients with probable Alzheimer’s disease is included.

Patients

Eighteen patients with dementia of the Alzheimer type, according to the NINCDS-ADRDA criteria (McKhann et al. 1984) for “probable Alzheimer’s disease,” were studied. The median age was 70 years (range, 58–83 years), and the median duration of disease was 3 years (range, 0.5–10 years). All patients underwent an extensive study program — including at least one interview of the patient and relatives, neurological examination, neuropsychological tests, laboratory tests, and a computer tomography (CT) scan — to exclude other possible causes of dementia. The CT scans were all normal, except for atrophy. The severity of dementia was graded by the Mini-Mental-State (Folstein et al. 1975), which has a maximum score of 30. The median Mini-Mental-State score was 16 (range, 3–27). Informed consent to participate in the study, which was approved by the local ethical committee, was obtained from the patient and a close relative.

Methods

One vial with unlabeled $d,l$-HMPAO (Ceretec) was mixed with fresh eluent from a $^{99m}$Tc generator in daily use. A 10-ml bolus with 1.1 GBq $[^{99m}$Tc$]$-$d,l$-HMPAO