# Technetium HMPAO SPECT Study in Dementia with Lewy Bodies, Alzheimer's Disease and Idiopathic Parkinson's Disease

Luc J.P. Defebvre, Valérie Leduc, Alain Duhamel, Pascal Lecouffe, Florence Pasquier, Chantale Lamy-Lhullier, Marc Steinling and Alain Destée

*Departments of Neurology A, Medical Informatics, Nuclear Medicine and Memory Center, Lille, France*

The aim of this study was to compare the regional cerebral blood flow measurements studied by SPECT in dementia with Lewy bodies (DLB) and Alzheimer's disease (AD) to determine the contribution of SPECT to the differential diagnosis of these two diseases. **Methods:** SPECT analysis with $^{99m}$Tc-hexamethyl propyleneamine oxime (HMPAO) was performed in 20 patients with probable DLB, 20 patients with probable AD and 20 patients with idiopathic Parkinson's disease (IPD). Ten pairs of regions of interest were analyzed. Tracer uptake was expressed as a corticocerebellar activity ratio. **Results:** Compared with IPD, in the DLB group there was a global decrease of HMPAO uptake in cortical regions of interest except in the posterior frontal and occipital regions; in the AD group there was limited left temporal and parietal hypoperfusion. In the DLB group, frontal HMPAO uptake was significantly lower than in the AD group. Two predictive scores were established by a factorial discriminant analysis from six left cortical indices (medial frontal, lateral frontal, posterior frontal, temporoparietal, parietal and parietooccipital) and the Mini-Mental State Examination, which correctly classified 53 of 60 patients (88%) (DLB, 18 of 20; AD, 16 of 20; IPD, 19 of 20). **Conclusion:** These findings indicate the presence of diffuse cortical abnormalities in DLB and suggest that SPECT may be useful in discriminating in vivo DLB from AD, revealing mainly frontal hypoperfusion in the former group. We estimate that SPECT study increases the possibility of separating DLB and AD because both disorders share different patterns of cerebral blood flow abnormality.

**Key Words:** dementia with Lewy bodies; Alzheimer's disease; Parkinson's disease; SPECT; $^{99m}$Tc-hexamethyl propyleneamine oxime

**J Nucl Med 1999; 40:956–962**

Dementia with Lewy bodies (DLB) has been established as the most common senile degenerative dementia after Alzheimer's disease (AD) (*1–3*). Clinical diagnostic criteria for DLB have been defined (*3*), refining previous criteria (*4,5*). The central feature required for a diagnosis of DLB is a progressive and fluctuating cognitive decline with recurrent visual hallucinations, systematized delusions and spontaneous parkinsonian symptoms. Repeated falls, syncope, transient loss of consciousness and neuroleptic sensitivity are also useful clinical characteristics. In AD, the progressive decline of memory is prominent whereas neuropsychiatric features usually occur in the later stages (*6*). Moderate parkinsonian signs can be observed during AD evolution, as in DLB evolution (*7*). In some cases, the clinical distinction of patients with DLB and those with AD may be difficult because of overlapping symptoms such as cognitive decline, psychiatric signs and parkinsonian symptoms. When the initial presentation of DLB is characterized by impaired cognition, it can mimic AD (*2,8*). Furthermore, neuropsychological evaluation can disclose severe but similar degrees of impaired performances concerning attention, frontal lobe function and motor sequencing in both DLB and AD (*9*).

Pathological study remains the only way to confirm the diagnosis of DLB, when evidence of Lewy bodies is found in the cortex, the subcortical regions (nucleus basalis of Meynert) and the brain stem (substantia nigra and locus coeruleus) (*2,10–12*). The presence of Lewy bodies is the essential feature in the pathological diagnosis of DLB; other features (e.g., plaques and neuronal loss) can also be described in most but not in all cases (*3*). Consensus guidelines for brain sampling, evaluation of Lewy bodies (distribution and frequency) and diagnostic rating protocol have been proposed (*3*).

The precise nosological relationship of DLB and AD is still a matter of debate. On the one hand, the links with AD are often discussed because of the common clinical characteristics of the dementia and the lesions of Alzheimer type frequently observed in anatomopathological examination (*2*); on the other hand, other authors consider the two diseases independent (*13,14*), with DLB corresponding to a more extended form of idiopathic Parkinson's disease (IPD). DLB and IPD could then be the two extremes of a continuum (*15*).

With the perspective of neuroprotective treatments, early diagnosis is becoming an important factor. The more extensive cholinergic deficit (*8,16*) observed in DLB compared with AD explains the beneficial effect of cholinergic therapy

Received Apr. 14, 1998; revision accepted Jan. 4, 1999.

For correspondence or reprints contact: Luc J.P. Defebvre, MD, PhD, Service de Neurologie et Pathologie du Mouvement, Hôpital Roger Salengro, CHRU, 59037 Lille, France.

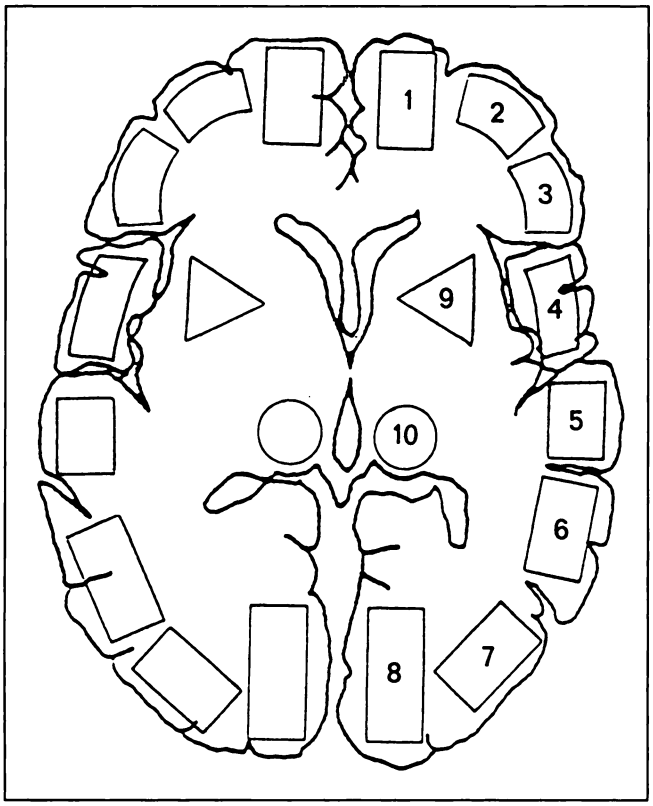


**FIGURE 1.** Ten pairs of regions of interest, right and left: medial frontal (1), lateral frontal (2), posterior frontal (3), temporoinsular (4), temporoparietal (5), parietal (6), parietooccipital (7), occipital (8), lenticular nucleus (9) and thalamus (10).

in DLB (cholinesterase inhibitor), which improves impaired cognitive functions (*17*). An early marker of the diagnosis would be of the greatest interest, because the reliability of clinical and pathological criteria of DLB are undergoing evolution without complete specificity (*18*). Thus, noninvasive imaging with PET or a more widely available technique such as SPECT may be useful methods for the diagnosis of dementing disorders.

The abnormal pattern of regional cerebral blood flow (rCBF) characteristic of AD is a bilaterally decreased perfusion to the temporal and parietal regions (*19,20*). However, heterogeneous patterns of rCBF deficits have been seen with SPECT. This heterogeneity may reflect different stages of the disease or cognitive subtypes (*21*). In DLB, a temporoparietal hypoperfusion has recently been shown associated with an occipital hypoperfusion, which could explain the visual hallucinations (*22*).

The aim of this study was to compare the rCBF measurements studied by SPECT with $^{99m}$Tc-hexamethyl propyleneamine oxime (HMPAO) in DLB, AD and IPD to determine the contribution of SPECT to the differential diagnosis of DLB and AD.

## MATERIALS AND METHODS

### Patients

SPECT data were collected from 20 patients with probable DLB according to the consensus guidelines for the clinical diagnosis of DLB (*3*) (mean age 67.6 ± 9.8 y, mean disease duration 6.0 ± 3.4 y); 20 patients with probable AD according to the National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria (*6*) (mean age 71.4 ± 5.2 y, mean disease duration 6.2 ± 2.4 y); and 20 patients with IPD based on the United Kingdom Parkinson's Disease Society brain bank criteria (*23*) (mean age 66.1 ± 6.0 y, mean disease duration 4.8 ± 3.0 y). With a one-way analysis of variance (ANOVA), the duration of the disease did not differ significantly between the three groups (at level 5%). The mean age was significantly higher in the AD group than in the IPD group.

Patients with a history of psychiatric disorders or other neurological disorders (including dysthyroidism, vitamin $B_{12}$ or folate deficiency, cerebrovascular disease) were excluded. Patients were free from psychotropic medications (anxiolytic, antidepressant, neuroleptic). CT scans and MR images were negative for stroke. Each patient's cognitive impairment was graded by the Mini-Mental State Examination (MMSE) (*24*). In DLB patients, the MMSE score (mean ± SD) was 16 ± 6; in AD patients, it was 18 ± 7; and in IPD patients, it was 25 ± 3. MMSE scores were significantly lower in the DLB and AD groups compared with the IPD group; the difference was not significant between the DLB and AD groups.

### SPECT Methodology

SPECT was performed with a brain-dedicated fast-rotating SPECT system, the Tomomatic 564 (Medimatic, Copenhagen,

**TABLE 1**
Mean Values ± SD of Different Cerebral Blood Flow Indexes Obtained in Three Groups

| Group | Left med-fr | Right med-fr | Left lat-fr | Right lat-fr | Left post-fr | Right post-fr |
|---|---|---|---|---|---|---|
| DLB | 0.79 ± 0.05 | 0.79 ± 0.04 | 0.74 ± 0.04 | 0.76 ± 0.06 | 0.79 ± 0.05 | 0.80 ± 0.05 |
| AD | 0.84 ± 0.07 | 0.85 ± 0.07 | 0.83 ± 0.07 | 0.84 ± 0.07 | 0.87 ± 0.07 | 0.88 ± 0.06 |
| IPD | 0.86 ± 0.07 | 0.87 ± 0.08 | 0.80 ± 0.06 | 0.81 ± 0.05 | 0.83 ± 0.06 | 0.85 ± 0.06 |
| Statistical results | DLB/AD DLB/IPD | DLB/AD DLB/IPD | DLB/AD DLB/IPD | DLB/AD DLB/IPD | DLB/AD | DLB/AD |

med-fr = medial frontal; lat-fr = lateral frontal; post-fr = posterior frontal; DLB = dementia with Lewy bodies; AD = Alzheimer's disease; IPD = idiopathic Parkinson's disease.

Statistical difference: The multiple comparison of means was performed using Bonferroni's correction ($\alpha/3$ with $\alpha = 0.05$). For each region of interest, the groups that are significantly different are specified. DLB/AD indicates a significant difference between the DLB and AD groups. DLB/IPD indicates a significant difference between the DLB and IPD groups.

**TABLE 2**
Mean Values ± SD of Different Cerebral Blood Flow Indexes Obtained in Three Groups

| Group | Left temp-ins | Right temp-ins | Left temp-par | Right temp-par | Left par | Right par |
|---|---|---|---|---|---|---|
| DLB | 0.81 ± 0.07 | 0.85 ± 0.04 | 0.81 ± 0.06 | 0.84 ± 0.05 | 0.76 ± 0.05 | 0.76 ± 0.06 |
| AD | 0.88 ± 0.07 | 0.88 ± 0.06 | 0.84 ± 0.11 | 0.89 ± 0.08 | 0.77 ± 0.12 | 0.82 ± 0.10 |
| IPD | 0.87 ± 0.04 | 0.90 ± 0.06 | 0.90 ± 0.04 | 0.92 ± 0.04 | 0.84 ± 0.05 | 0.85 ± 0.06 |
| Statistical results | DLB/AD DLB/IPD | DLB/IPD | DLB/IPD AD/IPD | DLB/AD DLB/IPD | DLB/IPD AD/IPD | DLB/AD DLB/IPD |

temp-ins = temporoinsular; temp-par = temporoparietal; par = parietal; DLB = dementia with Lewy bodies; AD = Alzheimer's disease; IPD = idiopathic Parkinson's disease.

Statistical difference: The multiple comparison of means was performed using Bonferroni's correction ($\alpha/3$ with $\alpha = 0.05$). For each region of interest, the groups that are significantly different are specified. DLB/AD indicates a significant difference between the DLB and AD groups. DLB/IPD indicates a significant difference between the DLB and IPD groups. AD/IPD indicates a significant difference between the AD and IPD groups.

Denmark), about 10 min after intravenous administration of a freshly prepared saline bolus of 550 MBq $^{99m}$Tc-HMPAO. Patients lay with their eyes closed in a quiet dark room. The head was carefully placed along the canthomeatal line using a three-laser light-positioning system. A first test acquisition (60 s) was performed to control and, if necessary, to adjust the position of the head of the patient. Two series of five 15-mm-thick slices with a center-to-center distance of 10 mm and parallel to the canthomeatal plane were obtained. Each series required a duration of 10 min and 2 million counts could be obtained in the medium slice. Reconstruction was performed using a filtered backprojection. We used an autogauss filter (DC amplification 80%; power of truncation 3; accepted noise level 3%). A correction for attenuation was performed using a value of 0.16 $cm^{-1}$.

Ten pairs of regions of interest (ROIs) were drawn in conformity with the Cabanis Atlas (*25*) on a slice located 50 mm above the orbitomeatal plane. Size of the ROI depends on the region: Ranges were between 1.9 $cm^2$ for the frontal ROI and 5.5 $cm^2$ for the occipital ROI. These right and left ROIs were specified in Figure 1. Tracer uptake was expressed as a corticocerebellar activity ratio, so that cerebellar hemispheres were used (slice located on the orbitomeatal plane) as the particular reference of the patient, using a method previously described (*26*).

### Statistical Analysis

All statistical analyses were performed using SAS software (SAS Institute, Inc., Cary, NC). Data are expressed as mean and SD. Unless otherwise stated, the statistical tests were made at the 0.05 level. For the SPECT data, the assumption of normality was assessed using the Shapiro-Wilk test (*27*). The individual predictive value of each parameter related to the 10 pairs of ROIs. The MMSE score was first examined by a one-way ANOVA and multiple comparisons of means were performed using the Bonferroni's correction. A factorial discriminant analysis (FDA) was performed with the parameters having a significance level less than 15%. FDA is a multivariate statistical procedure that uses a set of explanatory variables to classify patients into different subgroups (in this study, the AD, IPD and DLB subgroups) by specific rules. FDA allows two new variables, the predictive scores, which are linear combinations of the explanatory variables. These scores maximize the ratio of the variability between the groups to the variability within the groups, and therefore patients of different groups have scores as different as possible. The scores are used to determine the classification rules. Subsequently, to select the best subset of predictor variables, we performed a stepwise discriminant analysis (at level 15% with stepwise option, which is a forward selection allowing elimination). The results of the rules were assessed by the classification table.

## RESULTS

The descriptive analysis showed that the distribution of each CBF index was compatible with the normality assumption. The mean CBF indices ± SD obtained in the three groups are reported in Tables 1–3. Six parameters were excluded after the one-way ANOVA: right and left occipital, lenticular nucleus and thalamus (because there was no statistical difference at the 0.15 level among the three

**TABLE 3**
Mean Values ± SD of Different Cerebral Blood Flow Indexes Obtained in Three Groups

| Group | Left par-occ | Right par-occ | Left occ | Right occ | Left lent | Right lent | Left thal | Right thal |
|---|---|---|---|---|---|---|---|---|
| DLB | 0.78 ± 0.06 | 0.77 ± 0.06 | 0.94 ± 0.07 | 0.95 ± 0.07 | 0.91 ± 0.06 | 0.91 ± 0.05 | 0.86 ± 0.06 | 0.85 ± 0.07 |
| AD | 0.79 ± 0.11 | 0.82 ± 0.10 | 0.97 ± 0.07 | 0.99 ± 0.07 | 0.95 ± 0.07 | 0.96 ± 0.06 | 0.88 ± 0.06 | 0.88 ± 0.07 |
| IPD | 0.82 ± 0.04 | 0.83 ± 0.04 | 0.98 ± 0.04 | 0.99 ± 0.04 | 0.92 ± 0.06 | 0.93 ± 0.06 | 0.88 ± 0.05 | 0.89 ± 0.05 |
| Statistical results | DLB/IPD | DLB/IPD | NS | NS | NS | NS | NS | NS |

par-occ = parietooccipital; occ = occipital; lent = lenticular nucleus; thal = thalamus; DLB = dementia with Lewy bodies; AD = Alzheimer's disease; IPD = idiopathic Parkinson's disease; NS = not significant.

Statistical difference: The multiple comparison of means was performed using Bonferroni's correction ($\alpha/3$ with $\alpha = 0.05$). For each region of interest, the groups that are significantly different are specified. DLB/IPD indicates a significant difference between the DLB and IPD groups.

groups). In the IPD group, the ROI indices were normal: all the mean values of each ROI were superior to 0.80 (*26,28*). Compared with IPD, in the AD group there was a limited left temporoparietal and parietal reduction of the HMPAO uptake, and in the DLB group there was a global and bilateral decrease of uptake in all cortical ROIs except in the posterior frontal and occipital regions. Comparison of the two demented groups revealed in the DLB group a hypoperfusion in all frontal regions and in the left temporoinsular, right temporoparietal and parietal regions.

The FDA performed on 15 parameters (MMSE score and 14 indices: all except for the right and left occipital lobes, lenticular nucleus and thalamus) showed a good separation among the three groups by means of the two discriminant scores ($S_1$ and $S_2$). The squared correlation ratio (CR) of these scores (ratio of the interclass–class variance to the total variance) was $CR_1 = 0.70$ ($S_1$) and $CR_2 = 0.5$ ($S_2$), respectively. Using Mahalanobis distance, we correctly classified 93% (56/60) of the patients. The IPD group was distinguished from the DLB and AD groups by means of $S_1$. The most discriminant parameters associated with $S_1$ were MMSE ($r = 0.68$), left temporoparietal ($r = 0.46$) and left parietal ($r = 0.46$) ($r$ denotes the Pearson correlation coefficient between the variable and the score $S_1$). $S_2$ distinguished DLB and AD groups and the corresponding discriminant variables were left lateral-frontal ($r = 0.76$), right lateral-frontal ($r = 0.73$), left posterior-frontal ($r = 0.67$) and right posterior ($r = 0.68$).

The following predictor variables were definitively retained after the stepwise discriminant analysis: MMSE, left medial-frontal, left lateral-frontal, left posterior-frontal, left temporoparietal, left parietal and left parietooccipital. A second FDA was performed on these seven remaining parameters. The results are presented in Tables 4 and 5 and Figure 2. The correlation ratios of the two scores derived from the FDA were $CR_1 = 0.6$ and $CR_2 = 0.4$. Table 4 shows how these two scores can be computed from the seven predictors. Figure 2 represents the projection of the 60 patients in the $S_2 \times S_1$ plane. On this plot, the first coordinate is defined by the $S_1$ value and the second coordinate is defined by the $S_2$ value, both computed from Table 4. Figure 2 demonstrates that the subset of seven variables seemed to be relevant for predicting diagnosis. Then, from Figure 2, three decision rules were derived: (a) if $S_1 < 0$, then diagnosis = IPD; (b) if $S_1 > 0$ and $S_2 \geq 0$, then diagnosis = AD; (c) if $S_1 > 0$ and if $S_2 < 0$, then diagnosis = DLB. Consider, for example, a patient with the following SPECT characteristics: left medial-frontal = 0.88, left lateral-frontal = 0.75, left posterior-frontal = 0.79, left temporoparietal = 0.73, left parietal = 0.7, left parietal-occipital = 0.7, MMSE = 11. By computing the two score values and by using the two rules, this patient would be classified in the DLB group ($S_1 = +1$, $S_2 = -1.35$).

Table 5 gives the result of the classification obtained using the two decision rules. Of the 60 patients, 88.3% were correctly classified: 90% for the DLB group, 80% for the AD group and 95% for the IPD group.

**TABLE 4**
Coefficient Values Obtained by Factorial Discriminant Analysis Computing Scores 1 and 2 According to the Seven Predicting Factors

| Parameters | Score 1 | Score 2 |
|---|---|---|
| Mini-Mental State Examination | −0.1 | 0 |
| Left medial-frontal index | −12.5 | −1.2 |
| Left lateral-frontal index | 0 | +12.2 |
| Left posterior-frontal index | +18.7 | +7.3 |
| Left temporoparietal index | −4.2 | +5.3 |
| Left parietal index | −8.4 | −6.9 |
| Left parietooccipital index | +10 | −3.5 |
| Constancy | +0.3 | −11.8 |

**TABLE 5**
Predictive Results for Whole Population According to Predicting Factors Obtained with Factorial Discriminant Analysis

| Prediction | Diagnosis | | |
|---|---|---|---|
| | DLB | AD | IPD |
| DLB | 18 | 2 | 1 |
| AD | 2 | 16 | 0 |
| IPD | 0 | 2 | 19 |
| Correctly classified | 90% | 80% | 95% |

DLB = dementia with Lewy bodies; AD = Alzheimer's disease; IPD = idiopathic Parkinson's disease.
All together, 88.3% were correctly classified.

## DISCUSSION

In this study, we found a diffuse cortex reduction of HMPAO uptake in DLB patients compared with parkinsonian and AD patients for the same grade of cognitive impairment in the DLB and AD groups, whereas there was no significant difference for duration of the disease. Moreover, a clear distinction among the three groups was established with the FDA. The diffuse decrease of HMPAO cerebral uptake observed in the DLB group compared with the IPD group suggests widespread lesions in the cortex, as has been demonstrated in pathological studies (cortical Lewy bodies are observed in many cortical structures especially in the frontal, anterior cingulate, insular and temporal cortex) (*8,11,29*).

In IPD, cortical metabolism abnormality depends on disease duration and presence or absence of dementia: In the first stage of the disease, there is no change of glucose metabolism (*30*), whereas a significant global hypometabolism may appear a few years later (*31*). Piert et al. (*32*) showed a global reduction of glucose utilization in Parkinson's disease (mean reduction 22%) with a greater deficit across the brain with progression of the disease and development of dementia, especially in the parietal and occipital cortex. A marked parietal glucose hypometabolism, as

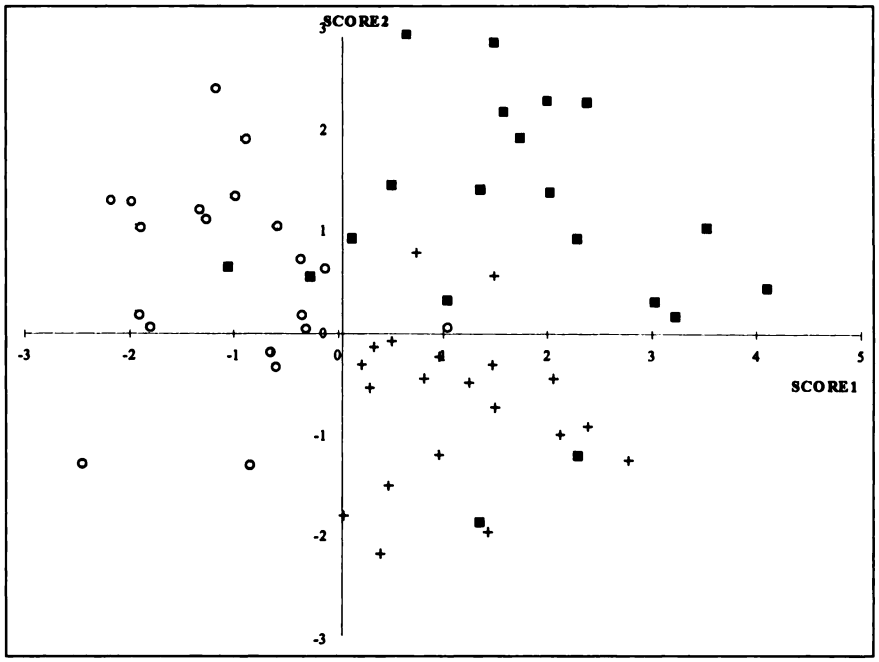


**FIGURE 2.** Separation of three groups of patients by discriminant scores $S_1$ and $S_2$. + = DLB; ■ = AD; ○ = IPD.

observed in AD, has been noted as the primary difference between Parkinson's disease and Parkinson's disease with dementia (*31*). However, in such studies, recent clinical criteria were not used to distinguish DLB. In our IPD group, no patients were demented, which is consistent with the normality of the ROI indices (superior to 0.8). In AD, the most marked rCBF defect using the radionucleotide HMPAO is localized in posterior cortical regions bilaterally (*19*); however, left hemispheric uptake decrease has been found to be more severe (*33*), which explains why there was only a left temporal and parietal uptake reduction in the AD group compared with the IPD group in our study.

A recent SPECT study compared the brain perfusion (visual analysis) of six patients with probable AD to that of seven patients with DLB (*22*). Compared with three controls, there was a bilateral temporal or parietal hypoperfusion for all AD patients with additional frontal hypoperfusion in two patients and an occipital defect in one patient. In the DLB group, there was, in addition to a temporoparietal HMPAO uptake decrease, an occipital hypoperfusion in six patients. Varma et al. (*34*) observed that the mean cortical CBF indices were lower in DLB (20 patients; mean duration of disease 4.3 y) and AD (57 patients; mean duration of disease 3.6 y) than in controls. The decrease was similar and symmetrical in the two groups and was most pronounced in posterior cortical ROI. However, there was a significantly smaller degree of variance in the left-right CBF asymmetry parameter for the DLB group. Taking into account the clinical onset (parkinsonian or cognitive-psychiatric symptoms), no difference for the CBF results was observed within the DLB group. The more diffuse decrease of regional cerebral perfusion observed in our DLB group in comparison with the study of Donnemiller et al. (*22*) can be explained by the fact that the dementia was more severe in our patients (mean MMSE score 16 ± 6) than in their patients (mean MMSE score 20 ± 5).

In the same way, a fluorodeoxyglucose (FDG) PET study provided evidence of diffuse cerebral hypometabolism (frontal, temporal and parietal) in both pure DLB (3 patients) and combined DLB-AD (3 patients) patients with a marked decline in parietal cortex, sparing the primary somatomotor cortex and subcortical strutures (*35*). An occipital hypometabolism was also found in both occipital association and primary visual cortex and might be related to the visual hallucinations classically observed in DLB, although the occipital lobe may be relatively spared in pathological analysis (*35–37*). Minoshima et al. (*38*) also observed similar metabolic reduction of FDG in AD patients with (n = 10) and without (n = 7) cortical Lewy bodies in multiple brain regions—including parietal, temporal and frontal cortex—with a significant severe reduction in the occipital cortex for the first group (−25% of controls) as compared with the other group (−10%), suggesting that this occipital defect may serve as an in vivo indicator for the presence of cortical Lewy bodies. However, this occipital hypometabolism is observed not only in DLB but in AD patients (*39,40*) and consequently does not seem to be useful for distinguishing the metabolic pattern of these two diseases.

The comparison between our two demented groups essentially revealed a hypoperfusion in all frontal regions in the DLB group and seems to confirm, on the contrary, that frontal CBF uptake is more sensitive for distinguishing in vivo DLB and AD. This HMPAO uptake decrease could be explained by the high density of cortical Lewy bodies sometimes observed in the frontal cortex (*8*). Finally, it can be assumed that CBF abnormalities in DLB patients reflect a combination of direct cortical pathology and cortical deaffer-

entation phenomenon secondary to subcortical lesions. The subcortical dysfunction can also be estimated by using $^{123}$I 2β carboxymethoxy-3β-[4-iodophenyl]tropane ($^{123}$I-β-CIT): A lower striatal-to-cerebellar ratio of $^{123}$I-β-CIT binding has been demonstrated in DLB patients compared with AD patients and controls (*22*), in accordance with the known severe nigrostriatal degeneration in DLB. Some of the limits of our methodology must be specified. Use of HMPAO gives an instantaneous assessment of local cerebral perfusion limited to a qualitative or semiquantitative approach. Index values also depend on the choice of the reference; the following references were used the most: cerebellar hemispheres, global hemisphere activity and occipital region. Criticisms can be made for all these references; however, we have already established that the cerebellar reference was the best one (*28*). ROIs were determined on a single slice only (50 mm above the orbitomeatal plane) and they did not allow extensive estimation of the CBF activity of the different cortical regions; however, a predictive score could be obtained rapidly and simply with this method. Our system had poor resolution and, at times, we encountered some difficulties when measuring HMPAO uptake in subcortical regions of small volume (thalamus and lenticular nucleus). This probably explains in part why no difference was observed among the three groups for these regions in our study. It would be interesting to use other markers such as $^{123}$I-β-CIT (*28*) or $^{123}$I-iodobenzamide (*41*) to analyze the subcortical dysfunction for distinguishing DLB and AD in patients.

## CONCLUSION

We consider that SPECT study increases the possibility of distinguishing between DLB and AD, because both disorders share different patterns of CBF abnormality. Our data suggest that the rCBF cortical changes observed in patients with parkinsonian syndrome and dementia could constitute a possible means of investigation in vivo for establishing a differential diagnosis of DLB and AD. A prospective longitudinal study will be required to define the role of such SPECT studies in obtaining a more precise diagnosis at the first stage of the evolution. The accurate clinical differentiation of DLB and AD is important to patient management, long-term prognosis and critical evaluation of future treatments.

## REFERENCES


1. Byrne EJ, Lennox G, Lowe J, Godwin-Austen R. Diffuse Lewy body disease: clinical features in 15 cases. *J Neurol Neurosurg Psychiatry.* 1989;52:709–717.
2. Hansen L, Salmon D, Galasko D, et al. The Lewy body variant of Alzheimer's disease: a pathological and clinical entity. *Neurology.* 1990;40:1–8.
3. McKeith IG, Galasko D, Kosaka K, et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium of DLB international workshop. *Neurology.* 1996;47:1113–1124.
4. Byrne EJ, Lennox GG, Godwin-Austen RB, et al. Dementia associated with cortical Lewy bodies: proposed clinical diagnostic criteria. *Dementia.* 1991;2:283–284.
5. McKeith IG, Fairbain A, Perry RH. Clinical diagnostic criteria for Lewy body dementia. *Dementia.* 1992;3:251–252.
6. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. *Neurology.* 1984;34:939–944.
7. Soininen H, Laulumaa V, Helkala EL, Hartikainen P, Rieckkinen PJ. Extrapyramidal signs in Alzheimer's disease: a 3-year follow-up study. *J Neural Transm.* 1992;4:107–119.
8. Förstl H, Burns A, Luther P, Cairns N, Levy R. The Lewy body variant of Alzheimer's disease: clinical and pathological findings. *Br J Psychiatry.* 1993;162:385–392.
9. Gnanalingham KK, Byrne EJ, Thornton A, Sambrook MA, Bannister P. Motor and cognitive function in Lewy body dementia: comparison with Alzheimer's and Parkinson's diseases. *J Neurol Neurosurg Psychiatry.* 1997;62:243–252.
10. Kosaka K, Yoshimura M, Ikeda K, Budka H. Diffuse type of Lewy body disease: progressive dementia with abundant cortical Lewy bodies and senile changes of varying degree — a new disease? *Clin Neuropharmacol.* 1984;3:185–192.
11. Gibb WR, Luthert PJ, Janota I, Lantos PL. Cortical Lewy body dementia: clinical features and classification. *J Neurol Neurosurg Psychiatry.* 1989;52:185–192.
12. Kosaka K. Diffuse Lewy body disease in Japan. *J Neurol.* 1990;237:197–204.
13. Dickson DW, Crystal HA, Davies P, Hardy H. Cytoskeletal and Alzheimer-type pathology in Lewy body disease. In: Perry R, McKeith I, Perry E, eds. *Dementia with Lewy Bodies. Clinical, Pathological and Treatment Issues.* Cambridge, UK: Cambridge University Press; 1996:224–237.
14. Kosaka K, Iseki E. Diffuse Lewy body disease within the spectrum of Lewy body disease. In: Perry R, McKeith I, Perry E, eds. *Dementia with Lewy Bodies. Clinical, Pathological and Treatment Issues.* Cambridge, UK: Cambridge University Press; 1996:238–247.
15. Filley CM. Neuropsychiatric features of Lewy body disease. *Brain Cogn.* 1995;28:229–239.
16. Perry EK, Irving D, Kerwin JM. Cholinergic transmitter and neurotrophic activities in Lewy body dementia: similarity to Parkinson's and distinction to Alzheimer's disease. *Alzheimer Dis Assoc Disord.* 1993;7:69–79.
17. Lebert F, Souliez L, Pasquier F. Tacrine and symptomatic treatment in Lewy body dementia. In: Perry R, McKeith I, Perry E, eds. *Dementia with Lewy Bodies. Clinical, Pathological and Treatment Issues.* Cambridge, UK: Cambridge University Press; 1996:439–448.
18. Mega MS, Masterman DL, Benso DF, et al. Dementia with Lewy bodies: reliability and validity of clinical and pathologic criteria. *Neurology.* 1996;47:1403–1409.
19. Neary D, Snowden JS, Shields RA, Burjan AWI, Northen B. Single photon emission tomography using $^{99m}$Tc-HMPAO in the investigation of dementia. *J Neurol Neurosurg Psychiatry.* 1987;50:1101–1109.
20. Jagust WJ, Johnson KA, Holman BL. SPECT perfusion imaging in the diagnosis of dementia. *J Neuroimag.* 1995;5(suppl):S45–S52.
21. Waldemar G, Bruhn P, Kristensen M, Johnsen A, Paulson OB, Lassen NA. Heterogeneity of neocortical cerebral blood flow deficits in dementia of the Alzheimer type: a $^{99m}$Tc-d,l-HMPAO SPECT study. *J Neurol Neurosurg Psychiatry.* 1994;57:285–295.
22. Donnemiller E, Heilmann J, Wenning GK, et al. Brain perfusion scintigraphy with $^{99m}$Tc-HMPAO or $^{99m}$Tc-ECD and $^{123}$I-β-CIT single-photon emission tomography in dementia of the Alzheimer-type and diffuse Lewy body disease. *Eur J Nucl Med.* 1997;24:320–325.
23. Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. *J Neurol Neurosurg Psychiatry.* 1992;55:181–184.
24. Folstein M, Folstein S, McHugh PR. Mini-Mental State: practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975;12:911–922.
25. Cabanis EA, Tamraz J, Iba-Zizen MT. Imagerie par résonance magnétique (IRM) de la tête à 0,5 Tesla. Atlas de corrélations anatomiques normales dans 3 dimensions, selon l'orientation du plan neuro-oculaire (PNO). *Feuillets de Radiologie.* 1986;26:309–416.
26. Steinling M, Mazingue A, Kassiostis P, et al. Le HmPaO-Tc comme indicateur du débit sanguin cérébral local: étude quantifiée comparée à la méthode par inhalation du Xenon 133. *Ann Radiol.* 1988;4:229–237.
27. Shapiro SS, Wilk MB. An analysis of variance test for normality (complete samples). *Biometrika.* 1965;52:591–611.
28. Steinling M, Leys D, Amegassi F, et al. Assessment of dementia with HMPAO-Tc: which is the best reference for the quantification? In: Schmidt HAE, Chambron J, eds. *Nuclear Medicine. Quantitative Analysis in Imaging and Function.* Strasbourg, France: Schattaueur; 1989:349–351.
29. Kosaka K. Lewy bodies in cerebral cortex. Report of three cases. *Acta Neuropathol.* 1978;42:127–134.
30. Rougemont D, Baron JC, Collard P, Bustany P, Comar D, Agid Y. Local cerebral glucose utilization in treated and untreated patients with Parkinson's disease. *J Neurol Neurosurg Psychiatry.* 1984;47:824–830.

31. Kuhl DE, Metter EJ, Riege WH. Patterns of local cerebral glucose utilization determination in Parkinson's disease by the [$^{18}$F]fluorodeoxyglucose method. *Ann Neurol.* 1984;15:419–424.
32. Piert M, Koeppe RA, Giordani B, Minoshima S, Kuhl DE. Determination of regional rate constants from dynamic FDG PET studies in Parkinson's disease. *J Nucl Med.* 1996;37:1115–1122.
33. Pearlson GD, Harris GJ, Powers RE, et al. Quantitative changes in mesial temporal volume, regional cerebral blood flow, and cognition in Alzheimer's disease. *Arch Gen Psychiatry.* 1992;49:402–408.
34. Varma AR, Talbot PR, Snowden JS, Lloyd JJ, Testa HJ, Neary D. A $^{99m}$Tc-HMPAO single-photon emission computed tomography study of Lewy body disease. *J Neurol.* 1997;244:349–359.
35. Albin RL, Minoshima S, D'Amato CJ, Frey KA, Kuhl DA, Sima AAF. Fluoro-deoxyglucose positron emission tomography in diffuse Lewy body disease. *Neurology.* 1996;47:462–466.
36. Gibb WR, Eseiri MM, Lee AJ. Clinical and pathological features of diffuse cortical Lewy body disease (Lewy body dementia). *Brain.* 1985;110:1131–1153.
37. McKeith IG, Fairbairn AF, Perry RH, Thompson P. The clinical diagnosis and misdiagnosis of senile dementia of Lewy body type (SDLT). *Br J Psychiatry.* 1994;165:324–332.
38. Minoshima S, Foster NL, Frey KA, et al. Metabolic differences in Alzheimer's disease with and without cortical Lewy bodies as revealed by PET [abstract]. *J Cereb Blood Flow Metab.* 1997;17:S437.
39. Hof PR, Bouras C, Constantinidis J, Morrison JH. Selective disconnection of specific visual association pathways in cases of Alzheimer's disease presenting with Balint's syndrome. *J Neuropathol Exp Neurol.* 1990;49:168–184.
40. Berthier ML, Leiguarda R, Starkstein SE, Sevlever G, Taratuto AL. Alzheimer's disease in a patient with posterior cortical atrophy. *J Neurol Neurosurg Psychiatry.* 1991;54:1110–1111.
41. Walker Z, Costa DC, Janssen AG, Walker RW, Livingstone G, Katona CL. Dementia with Lewy bodies: a study of post-synaptic dopaminergic receptors with iodine-123 iodobenzamide single-photon emission tomography. *Eur J Nucl Med.* 1997;24:609–614.