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# SPECT patterns in probable Alzheimer's disease

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**Abstract** The primary objective of this study was to test hypotheses about the relationship between HMPAO-SPECT findings and probable Alzheimer's disease (DAT) in a relatively large sample of patients diagnosed according to DSM-III-R. SPECT patterns of 20 controls and 116 DAT patients were investigated. Left and right frontal, temporal, parietal and occipital regions of the brain were rated as showing a hypoperfusion or not. A wide variety of patterns were found and these are described in detail below. In DAT patients, temporal and/or parietal regions were affected significantly more often (88%, $p > 0.001$) than frontal and/or occipital regions (70%). A bilateral temporoparietal pattern, which has been repeatedly reported as typical for DAT, was observed in 48% of DAT patients, but also in 25% of controls, and did not differentiate significantly between these two groups ($p > 0.05$). Conversely, more than three regions with hypoperfusion were observed significantly more often in DAT patients (48%, $p < 0.01$) than in controls (10%). In DAT patients, the number of regions with hypoperfusion correlated significantly with the score of the Mini Mental State Examination (MMSE, $r = 0.33$, $p < 0.001$). The frequency of at least one hypoperfusion was approximately equal in left and right hemispheres (77% vs. 73%, $p = 0.2$). The hypothesis that cognitive decline in DAT starts in the temporal regions was tested in 14 SPECT patterns showing only one region with hypoperfusion. In 12 of these patterns, a temporal region was in fact affected ($p < 0.001$). Whereas hypoperfusion in frontal areas was not accompanied by a significantly lower MMSE than when only temporoparietal regions were affected, MMSE scores were significantly lower when occipital regions were affected in addition to temporoparietal regions ($p < 0.05$). The clinical use of SPECT findings was tested in discriminating analyses with the MMSE and a delayed recall test as additional predictors of DAT. Whereas the MMSE and the delayed recall test differentiated significantly between DAT patients and controls, SPECT findings yielded no further differentiation. In conclusion, the theoretical and clinical implications of SPECT findings and their relationships to other physiological and psychological variables deserve further investigation.

**Key words** HMPAO-SPECT · Alzheimer's disease · Hypoperfusion

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## Introduction

Probable dementia of the Alzheimer type (DAT) is associated with changes in regional cerebral blood flow that can be detected using single photon emission computer tomography (SPECT) (Gemmel et al. 1987, Burns et al. 1989, Geany et al. 1990, Montaldi et al. 1990, Habert et al. 1991). The value of SPECT findings in the diagnosis of DAT is still a matter of debate. For instance, Poremba (1993) argues that there are no DAT-specific biological markers to date, whereas Volles (1991) notes that functional imaging such as PET and SPECT may identify DAT even in early stages of the disease when the CCT is still normal. The different views may be explained by the heterogeneity of findings which is itself probably due to differences in methods and samples. The samples especially vary in the severity of dementia, and the sizes of the groups investigated often seem rather low. The finding probably noted most often in DAT patients is bilateral temporoparietal hypoperfusion. This finding is confirmed by some early PET studies (Frackowiak et al. 1981, McGeer et al. 1986). However, unilateral hypometabolism may also occur, especially in early DAT (Salmon and Franck 1989)

and bilateral temporoparietal hypoperfusion is also found in Parkinson's disease with dementia (Kuhl et al. 1984, Holman et al. 1992, Salmon et al. 1993), vascular dementia (Kuwabara et al. 1990), and Creutzfeld-Jakob disease (Friedland et al. 1984). Recent studies show that bilateral temporoparietal hypoperfusion (with or without additional defects) characterises approximately 50–65% of DAT patients (Holman et al. 1992, Horn et al. 1995). Thus, the sensitivity of this hypoperfusion pattern seems low, but the specificity seems high, if Parkinson's disease with dementia can be excluded. Moreover, it seems unlikely that a certain pattern of hypoperfusion is characteristic for all stages of DAT.

Eberling et al. (1992) suggested – as many authors have done previously – that the temporal lobes are the first neocortical regions affected in DAT. Eberling's group observed temporal changes in mild and moderate DAT, whereas decline was only seen in other regions in moderate DAT. Wolfe et al. (1995) reported that the temporal lobe regional cerebral blood flow ratio – but not parietal or frontal ratios – predicts cognitive decline over a longitudinal follow-up. In criticism, it must be mentioned that Wolfe et al. (1995) used the ratio of region of interest to occipital cortex, and assumed the occipital cortex to be "relatively unaffected" by DAT. This assumption seems questionable, at least at later stages of DAT. Nevertheless, current evidence suggests that the role of the temporal lobes in the first stages of DAT deserves further investigation.

Besides the inherent methodological difficulties already mentioned, the evaluation of previous findings is complicated by the fact that most studies describe the observed perfusion patterns incompletely. The purpose of the current study is to evaluate hypoperfusion patterns in a relatively large sample of DAT patients, to describe them exhaustively and to test them in comparison to SPECT patterns of a control group of patients diagnosed as "normal". To our knowledge, this is the first study with more than 100 DAT patients. A detailed evaluation of hypoperfusion patterns that show only one region with hypoperfusion ("isolated patterns") describes the beginning of cortical deterioration in DAT. A predominant affection of temporal lobes in these isolated patterns was expected. A critical evaluation of the clinical value of SPECT patterns in the diagnosis of DAT leads to the question whether SPECT findings supply additional information compared to other well-established diagnostic techniques. We, therefore, performed discriminating analyses that tested whether SPECT findings enhance discrimination between controls and DAT patients beyond the level reached by evaluation of the Mini Mental State Examination (MMSE, Folstein et al. 1975) and two delayed verbal memory test. Delayed memory tests are known to be sensitive indicators of even mild DAT (Welsh et al. 1992).

## Method

### Diagnosis

First of all, thorough psychiatric and neurological examinations were conducted. Furthermore, the MMSE (Folstein et al. 1975), Hachinski Scale (Hachinski et al. 1975) and an extensive neuropsychological test battery were performed. DSM-III-R criteria (American Psychiatric Association 1987) were employed for diagnosis. Causes of dementia other than DAT were excluded by laboratory-chemical analyses, CCT/MRT, EEG, and extracranial and transcranial Doppler sonography. Patients with a Hachinski score greater than 4 or more than two lacunal infarctions in CCT or MRT were excluded under a probable diagnosis of a vascular or a mixed-type dementia.

### HMPAO-SPECT

Interictal brain SPECT imaging was performed 30 to 120 min after injection of 555-740 MBq $^{99m}$Tc-HMPAO. Four different types of SPECT acquisition systems were used: three different rotating gamma cameras: APEX 409 (Elscint, single head, A); DYNA-SCAN (Picker, dual-head, B); Genesys (ADAC, single-head, C). With an acquisition time of 20–30 min, 60 (A) or 64 (B and C) projections were acquired with a 64*64 matrix. A ring system has been used since 1992: CERASPECT system (Digital Scintigraphic Inc., D). The system works with three collimators rotating within a single crystal system iodide ring detector and acquires three views from three angles simultaneously. The acquisition time was 30 min. One hundred and twenty projections were acquired uisng a 512*64 matrix. Coronal, sagittal and transaxial (parallel to the orbitomeatel line) slices were calculated from the original transaxial slices and summed in order to obtain two (A/B/C) or four (D) pixel thick slices. Additionally, "thin" slices (one pixel thick, parallel to the long axis of the temporal lobes) were calculated for evaluation of the temporal lobes. Two experienced nuclear medicine physicians who were blind to diagnosis and neuropsychological test results rated the findings. Eight regions of interest were defined: left and right frontal, temporal, parietal and occipital lobes, and it was evaluated whether these regions showed a hypoperfusion or not.

### Assessment of cognitive performance

Although many neuropsychological tests were performed in this study, this article is restricted to the evaluation of the MMSE and two delayed word tests. Delayed word recall has been proven to be extremely sensitive in the detection of mild cases of DAT (Welsh et al. 1992). Two tests of delayed word recall of varying difficulty were employed in our sample. Thirty-five patients who seemed less handicapped at an initial interview heard and recalled a 15-item word list five times. A second 15-item list was then given and recalled. Afterwards, patients were asked to recall the first word list without additional presentation. After a 30 min interval, the first word list had to be recalled a seventh time and the number of correctly reproduced words was scored (delayed word recall of 15 items, DWR15). Fifty-nine patients who seemed more handicapped underwent a similar procedure, but with an eight-item word list. This list was presented and recalled five times and then had to be recalled after a 30 min interval (DWR8). Although it is a methodological weakness of this study that not both delayed recall tests (or at least the same one) were employed for all patients, the use of different lists and methods seemed clinically useful at the time of testing in order to adjust the testing procedure according to the severity of impairment.

### Hypotheses

Review of the literature led to formulation of the following hypotheses: 1. A bilateral temporoparietal pattern of hypoperfusion should

**Table 1** Sample description

| | DAT | Control |
|---|---|---|
| N | 116 | 20 |
| Age (mean ± std. dev.) | 66 ± 9 | 56 ± 10 |
| Sex (female/male) | 60/56 | 12/8 |
| MMSE (mean ± std. dev.) | 19.9 ± 5.4 | 28.8 ± 1.2 |

significantly differentiate between DAT patients and controls. 2. In DAT patients, temporal and parietal cortex should be affected more frequently than frontal and occipital cortex, and the frequency of affection of left and right hemispheres should be approximately equal. 3. In DAT patients, more regions of the brain should show hypoperfusion than in controls. 4. If SPECT shows only one region with hypoperfusion, then this region is expected to be temporal since it is assumed that this is the first cortical area affected. 5. If SPECT is clinically useful, then the discrimination between DAT patients and controls should improve after inclusion of SPECT findings in discriminating analyses with MMSE, DWR8 and DWR15 as predictors of diagnosis.

### Sample

The sample was recruited in the memory clinic of the psychiatric department of Bonn university hospital. One hundred and thirty-six patients had undergone a HMPAO-SPECT and were diagnosed according to the criteria of DSM-III-R as suffering from DAT (116) or not suffering from dementia (20) (Table 1). The controls of the latter group, however, reported at least some cognitive complaints – typically memory problems – which were the reason for their examination at the memory clinic.

### Statistics

First of all, a complete description of the observed hypoperfusion patterns in the 116 DAT patients and the 20 controls is given. Thus, the data may be used to test hypotheses other than the ones tested here or may be combined with data sets from other studies. Frequencies of patterns were tested with the binomial test. Associations between patterns, and between patterns and diagnoses, were tested with the Pearson $chi^2$-test and sometimes described with phi values. MMSE scores in different groups were tested with the *t*-test for independent samples and the predictive value of SPECT findings was evaluated by discriminating analyses using MMSE and delayed free recall as additional predictors. All statistical analyses were performed with SAS 6.03 for personal computers.

## Results

The following SPECT patterns were observed in the 116 DAT patients (Table 2). There were 16 patterns which were significantly more frequent than would be expected by chance. The multiple use of the binomial test in 50 patterns infers the risk that some of the "significantly" frequent patterns are significant by chance. Therefore, we would only like to comment on the patterns with a frequency of at least five before we draw some general conclusions. In 8.6% of the DAT patients, no hypoperfusion was detected. In 6.9%, only the left temporal lobe seemed to be affected. In 6.0%, all regions except the frontal ones showed hypoperfusion. In 4.3%, only the parietal and the occipital

**Table 2** Observed frequencies of SPECT patterns in 116 DAT patients

| Pattern[a] | Frequency | Relative frequency (%) | $p < 0.01$[b] |
|---|---|---|---|
| 00000000 | 10 | 8.6 | * |
| 00001000 | 1 | 0.9 | |
| 00001010 | 3 | 2.6 | * |
| 00001111 | 5 | 4.3 | * |
| 00010000 | 4 | 3.4 | * |
| 00010001 | 2 | 1.7 | |
| 00010100 | 2 | 1.7 | |
| 00011010 | 1 | 0.9 | |
| 00011100 | 1 | 0.9 | |
| 00011111 | 1 | 0.9 | |
| 00100000 | 8 | 6.9 | * |
| 00100010 | 1 | 0.9 | |
| 00101010 | 1 | 0.9 | |
| 00101100 | 1 | 0.9 | |
| 00101111 | 5 | 4.3 | * |
| 00110000 | 3 | 2.6 | * |
| 00110011 | 1 | 0.9 | |
| 00110101 | 1 | 0.9 | |
| 00111011 | 1 | 0.9 | |
| 00111100 | 5 | 4.3 | * |
| 00111111 | 7 | 6.0 | * |
| 01000100 | 3 | 2.6 | * |
| 01010000 | 2 | 1.7 | |
| 01010100 | 3 | 2.6 | * |
| 01010101 | 1 | 0.9 | |
| 01011111 | 3 | 2.6 | * |
| 01100000 | 1 | 0.9 | |
| 01110000 | 1 | 0.9 | |
| 01110101 | 1 | 0.9 | |
| 01111000 | 1 | 0.9 | |
| 01111100 | 2 | 1.7 | |
| 10000000 | 1 | 0.9 | |
| 10100000 | 1 | 0.9 | |
| 10100100 | 1 | 0.9 | |
| 10100101 | 1 | 0.9 | |
| 10101010 | 5 | 4.3 | * |
| 10101111 | 1 | 0.9 | |
| 10110000 | 1 | 0.9 | |
| 10111100 | 1 | 0.9 | |
| 11000000 | 3 | 2.6 | * |
| 11001000 | 2 | 1.7 | |
| 11001100 | 1 | 0.9 | |
| 11001111 | 3 | 2.6 | * |
| 11010000 | 2 | 1.7 | |
| 11011101 | 1 | 0.9 | |
| 11100000 | 1 | 0.9 | |
| 11110000 | 2 | 1.7 | |
| 11111000 | 1 | 0.9 | |
| 11111100 | 5 | 4.3 | * |
| 11111111 | 1 | 0.9 | |

[a] 0 denotes normal perfusion, 1 hypoperfusion; the strings are in the sequence left frontal lobe – right frontal lobe – left temporal lobe – right temporal lobe – left parietal lobe – right parietal lobe – left occipital lobe – right occipital lobe

[b] binomial test with equal prior probability of each pattern = 1/256

**Table 3** Observed frequencies of SPECT patterns in 20 controls

| Pattern[a] | Frequency | Relative frequency (%) |
|---|---|---|
| 00000000 | 5 | 25 |
| 00000100 | 2 | 10 |
| 00010000 | 1 | 5 |
| 00010100 | 2 | 10 |
| 00011100 | 1 | 5 |
| 00100000 | 1 | 5 |
| 00101000 | 2 | 10 |
| 00110000 | 1 | 5 |
| 00111100 | 1 | 5 |
| 01100000 | 1 | 5 |
| 01110000 | 1 | 5 |
| 10100000 | 1 | 5 |
| 11110011 | 1 | 5 |

[a] 0 denotes normal perfusion, 1 hypoperfusion; the strings are in the sequence left frontal lobe – right frontal lobe – left temporal lobe – right temporal lobe – left parietal lobe – right parietal lobe – left occipital lobe – right occipital lobe

regions were affected. In 4.3%, a similar pattern was observed: all regions except the frontal ones and the right temporal lobe seemed to be affected. In a further 4.3% of the DAT patients, only the temporal and parietal regions were affected. In a further 4.3%, all frontal, temporal and parietal regions showed hypoperfusion, whereas the occipital regions were spared. Thus, the predominant impression from Table 2 is that there is a wide variety of SPECT patterns in DAT. Of course, the patterns result from different stages of the disease and are not error free. However, it seems unlikely that even for different stages of DAT "the" typical pattern arises. The frequency of involvement of left and right hemispheres was approximately equal (77% and 73% respectively, $p = 0.2$, binomial test).

Table 3 shows the patterns observed in the 20 controls.

Of course, the relative frequencies given in Table 3 are rough estimates, with N being only 20. For this reason, we do not want to comment on the patterns in detail but would just like to mention that only 25% of the controls showed a SPECT pattern without any hypoperfusion.

## Is bilateral temporoparietal hypoperfusion DAT-sensitive and -specific?

One problem with the term "bilateral temporoparietal hypoperfusion" is that it is not clear exactly which patterns are being described with this expression. In fact, different authors using this term assume different patterns and it is difficult, if not impossible, to decide which definition is the most appropriate one. We, therefore, used different definitions ranging from extremely narrow to extremely broad and report the observed frequencies for DAT patients and controls in Table 4.

Table 4 shows that the extreme definitions are obviously not appropriate. Although we investigated only 20 controls – and, therefore, the chi$^2$-test for significant association may seem somewhat hard – this result shows that the association between bilateral temporoparietal hypoperfusion and DAT is at least not a very close one.

Another implication of the hypothesis of bilateral temporoparietal hypoperfusion in DAT patients is that temporal and parietal regions of the brain should be affected more often than frontal and occipital regions. In fact, 88% of our DAT patients showed at least one temporal or parietal hypoperfusion, whereas 70% showed frontal and/or occipital hypoperfusions. A binomial test showed that the frequency of temporal and/or parietal affection was significantly higher ($p < 0.001$) than the 70% observed in frontal and/or occipital regions. Nevertheless, the observed difference of only 18% again suggests that at least in later stages of DAT hypoperfusions are often not restricted to the temporoparietal regions.

If DAT cannot be characterised easily by a certain pattern of hypoperfusion, it could theoretically be assumed that the amount of hypoperfusion is perhaps decisive. Since only 10% of the controls showed hypoperfusions in more than three regions, this cut-off point was also used in DAT patients. 48% of the DAT patients had SPECT patterns with hypoperfusions in more than three regions and this criterion proved to be significantly associated with diagnosis ($p < 0.01$, chi$^2$-test). Fig. 1 shows the mean MMSE for the number of regions with hypoperfusion in DAT patients.

**Table 4** Observed frequencies of bilateral temporoparietal hypoperfusion in 116 DAT patients and 20 controls for different definitions of bilateral temporoparietal hypoperfusion

| Definition[a] | Classification | Patterns[b] | Relative frequency (%) | | *p* Chi$^2$-test |
|---|---|---|---|---|---|
| | | | DAT patients | Controls | |
| lt and rt and lp and rp and not (lf or rf or lo or ro) | Extremely narrow | 00111100 | 4 | 5 | 0.89 |
| lt and rt and lp and rp | Narrow | XX1111XX | 18 | 5 | 0.14 |
| (lt and rt) or (lp and rp) | Broad | XX1X1XXX<br>XXX1X1XX | 48 | 25 | 0.053 |
| lt or rt or lp or rp | Extremely broad | XX1XXXXX<br>XXX1XXXX<br>XXXX1XXX<br>XXXXX1XX | 87 | 75 | 0.12 |

[a] l = left, r = right, f = frontal, t = temporal, p = parietal, o = occipital
[b] 0 = normal perfusion, 1 = hypoperfusion, X = normal or hypoperfusion

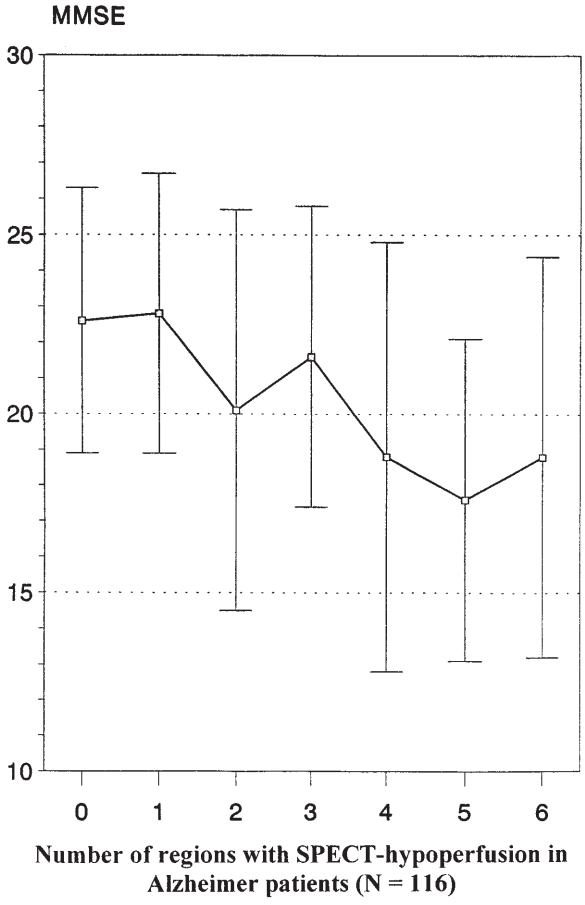


**Fig. 1** Means and standard deviations of the Mini Mental State Examination (MMSE, Folstein et al. 1975) for the number of regions with hypoperfusion in SPECT

There is a significant linear trend for the MMSE score to decrease with the number of regions with hypoperfusion ($r = 33$, $p < 0.01$).

To summarise, the data from this study show that the number of regions with hypoperfusion is more closely associated with DAT than the existence of any bilateral temporoparietal pattern. The severity of DAT as assessed with the MMSE is also significantly but not very closely related to the number of regions with hypoperfusions. Although these data suggest that the importance of bilateral temporoparietal hypoperfusion in DAT may have been overemphasised in the past, the importance of pattern analyses in general should not be renounced prematurely. The next section describes some more detailed analyses of the observed patterns.

## Does DAT start in the temporal regions?

The hypothesis that the cortical starting point of DAT is the temporal region is old, and in the meantime some data – including SPECT findings – have been acquired which seem to support this hypothesis (Eberling et al. 1992). One implication of this hypothesis that can be easily tested with the data from this study is that, if there is only one region with hypoperfusion, this should be a temporal one. Fourteen of our DAT patients showed only one region with hypoperfusion; the left temporal lobe was affected eight times and the right temporal lobe four times, whereas the left frontal and left parietal lobes were each affected only once. The probability of the observed accumulation in the temporal regions is $p < 0.001$ (binomial test with the assumption that hypoperfusions in all regions were equally probable = 1/8). This result strongly supports the hypothesis that the temporal region is usually the first one affected. Nevertheless, it must be mentioned that in the four controls who showed hypoperfusion in only one region, the temporal region was affected in two cases (and the right parietal region in two cases). Although the low N of controls necessitates care, this observation might suggest that the temporal regions may be especially vulnerable in general and not only for DAT. Although the left temporal lobe was affected twice as often as the right temporal lobe in this sample, this difference is not statistically significant with the low number of patterns showing only one region with hypoperfusion.

## Relationships between hypoperfusions in different areas

Table 5 shows phi coefficients for the associations between each pair of brain regions when 2*2 tables of the respective regions are statistically analysed. In this case, phi coefficients are comparable to correlations and can have values between – 1 and 1.

Especially the parieto-occipital region shows high and significant associations. A closer look at this region shows that if the left occipital lobe is affected, then in 95% of cases in this study the left parietal region is also affected. The respective relative conditional frequency for the right occipital region and the right parietal region is 89%. A

**Table 5** Association (phi coefficients) between hypoperfusions in different brain regions of N = 116 DAT patients

| | fr/l | fr/r | te/l | te/r | pa/l | pa/r | oc/l |
|---|---|---|---|---|---|---|---|
| fr/r | 0.41*** | | | | | | |
| te/l | 0.12 | –0.18* | | | | | |
| te/r | –0.10 | 0.23* | 0.14 | | | | |
| pa/l | 0.14 | –0.01 | 0.21* | 0.07 | | | |
| pa/r | –0.05 | 0.17 | 0.09 | 0.26** | 0.50*** | | |
| oc/l | –0.06 | –0.25** | 0.09 | –0.15 | 0.63*** | 0.26** | |
| oc/r | –0.13 | –0.08 | 0.02 | 0.11 | 0.38*** | 0.53*** | 0.65*** |

* $P < 0.05$, chi$^2$-test
** $P < 0.01$, chi$^2$-test
*** $P < 0.001$, chi$^2$-test
fr = frontal, te = temporal, pa = parietal, oc = occipital/l = left, r = right

plausible explanation for these associations is that after affection of the parietal regions, the ipsilateral occipital regions are affected next. All directly neighboured regions – ipsilateral and contralateral – with exception of the left frontal and temporal region and the left and right temporal region show significant associations. although these associations are clearly lower than in the parieto-occipital regions.

An interesting question is whether the additional involvement of the occipital region is accompanied by further functional decline. We, therefore, compared the MMSE scores of patients who showed only temporoparietal affection with those who also showed occipital affection. In fact, the first group had a significantly higher mean MMSE score (22.1) than the second group (18.3, $p < 0.05$, *t*-test). A similar analysis comparing the frontal with the temporoparietal region showed no significant difference. Thus, hypoperfusion in the occipital region seems to occur predominantly after affection of the parietal region and is accompanied by further cognitive decline.

### Do SPECT data contribute to the accuracy of diagnosis?

Thirteen of our controls and 22 of our DAT patients were tested with the MMSE and the more difficult delayed word recall test (DWR15). We performed discriminating analyses with MMSE and DWR15 as predictors. These variables discriminated significantly ($p < 0.05$) between diagnoses and classified 95% of DAT patients and 92% of controls correctly. Inclusion of the number of brain areas showing hypoperfusion as an additional predictor did not alter this result at all. Five of the controls and 54 of the DAT patients were tested with the MMSE and the easier delayed word recall test (DWR8). MMSE and DWR8 discriminated again significantly ($p < 0.05$) between diagnoses and classified 87% of DAT patients and 100% of controls correctly. Again, additional inclusion of the number of brain areas showing hypoperfusion did not improve classification. Thus, using only the MMSE and a delayed word recall test, good discrimination of diagnoses could be reached and there was no case in which this discrimination could be improved by taking the best discriminating SPECT variable into account. Although the N of controls is low, and therefore caution is necessary, in these data, SPECT findings are clearly outperformed by variables of cognitive function in their ability to differentiate between controls and DAT patients.

## Discussion

SPECT patterns observed in 20 controls and 116 DAT patients were evaluated. Although the temporal and parietal region showed hypoperfusion more frequently in DAT patients than the frontal and occipital region, bilateral temporoparietal hypoperfusion seems less characteristic for DAT than previously suggested. In these data, none of four different bilateral temporoparietal patterns was significantly associated with diagnosis. However, the most appropriate definition of bilateral temporoparietal hypoperfusion (bilateral temporal and/or parietal hypoperfusion with or without additional defects) led to patterns that only just missed significant association with diagnosis ($p = 0.053$). Moreover, the sample of controls was not large and is conspicuous in that the control patients – although finally diagnosed as "normal" – visited our memory clinic. Therefore, we feel sure that with a larger and/or less conspicuous sample of controls, a significant association between diagnosis and presence of bilateral temporoparietal hypoperfusion could be demonstrated. Nevertheless, a significant association does not mean that there is a close relationship, and in keeping with recent work (Holman et al. 1992, Horn et al. 1995), these data show that broadly defined bilateral temporoparietal hypoperfusion is found in only approximately 48% of DAT patients and also approximately 25% of controls with cognitive problems. In looking for an alternative SPECT indicator of DAT, the amount of hypoperfusions as indicated by the number of brain regions showing hypoperfusion was evaluated. This indicator – more than three regions with hypoperfusion – was significantly associated with diagnosis, and was more DAT-specific in this sample in that only 10% of the controls showed this feature. Moreover, in DAT patients the number of brain regions with hypoperfusion correlated significantly with the severity of dementia as measured by the MMSE. Nevertheless, further research is needed to decide whether this purely quantitative consideration of SPECT data, which completely ignores the location of hypoperfusion, is really an alternative or supplementation to other approaches.

In keeping with earlier publications (e.g. Eberling et al. 1992), the data from this study suggest that the cortical decline in DAT usually begins in the temporal regions: the temporal lobes were affected in 12 of the 14 cases which had hypoperfusion in only one region. If the occipital lobe was affected, then the ipsilateral parietal lobe was also affected in approximately 90% of cases. Hypoperfusion in the occipital lobe yielded significantly lower MMSE scores than in the temporoparietal region. Thus, in DAT final cortical involvement seems to extend usually from the parietal to the occipital lobe, accompanied by further cognitive impairment. Conversely, involvement of the frontal lobe did not significantly influence the MMSE score compared to the level that was observed with only temporoparietal affection.

DAT patients and controls could be well discriminated by the use of the MMSE and two delayed verbal recall tests (correct classification in about 90% of the cases). Additional inclusion of SPECT findings did not improve classification in any single case. Therefore, SPECT findings seem to be less useful than is sometimes suggested for the differentiation between controls and DAT patients. To the best of our knowledge, the performance of SPECT data in the differentiation of diagnoses has not yet been tested in comparison with other diagnostic tools.

To summarise, our results are not surprising if earlier and recent literature is evaluated critically. The diagnosis

of DAT remains primarily a clinical one, and the relationship between DAT and SPECT patterns is complex. Nevertheless, SPECT patterns contribute importantly to the description of changes in cerebral perfusion that are caused by DAT and other demential diseases. In this respect, HMPAO-SPECT can contribute valuable and clinically relevant information to other imaging approaches (Hampel et al. 1997) in the field of the aetiopathology and diagnosis of dementia.

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