Interictal brain ^{99m}Tc-HM-PAO SPECT hypoperfusion in patients with unstable partial epilepsy and normal CT

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Brain perfusion was studied interictally with ^{99m}Tc-HM-PAO SPECT in 47 adult patients with partial epilepsy and normal brain CT. Epilepsy was classified as secondarily generalized in 24 patients, as complex partial in 17 patients and as simple partial in 6 patients. In 24 patients good seizure control was not achieved as these patients had a median number of 78 seizures during the preceeding month, while in the rest of the patients seizure controll was relatively good (less than 6 seizures during preceeding month). Local brain hypoperfusion was observed in 41 or 87% of the patients. Hypoperfusion was located close to the EEG foci in 76% and equally often with temporal and frontal foci. Hypoperfusion and the EEG focus were located on the same side in 83%. Hypoperfusion was more frequent in secondarily generalized epilepsy and simple partial epilepsy than in complex partial epilepsy. Left-sided hypoperfusion was especially associated with complex partial epilepsy. It is likely that the significant epileptogenic brain area was revealed in patients with SPECT focus and EEG focus in the same brain area. In one of our patients MRI showed a small temporal lesion which on successful removal was identified as a low-grade oligodendroglioma. Abnormalities of regional brain uptake of HM-PAO demonstrated by SPECT in patients with partial epilepsy and normal brain CT give further information about pathophysiology in partial epilepsy; this may be of use both for selecting appropriate therapy and in presurgical localization of foci.

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Regional cerebral blood flow (rCBF) tomography by single photon emission computed tomography (SPECT) using lipophilic blood flow tracers has been established as a clinically useful examination in epilepsy (1), dementia (2), encephalitis (3), and stroke (4). In epilepsy, attention was initially focused on brain perfusion defects without regard to whether the anatomic defect was demonstrable on CT or not (5). Later, patients mostly with temporal epilepsy without any demonstrable structural abnormality in the brain have become the main objective for perfusion studies (6, 7). In such patients SPECT may reveal the laterization of the epileptogenic focus when other methods fail or contradict (7). SPECT may be the only routine imaging method capable of revealing focal abnormalities in epileptic syndromes, e.g. in Lennox-Gastaut syndrome (8). In presurgical localization of epileptic foci ictal scans have also proved valuable (9). Our aim was to study the diagnostic impact of ^{99m}Tc-HM-PAO rCBF SPECT on patients, many with bad seizure control, having normal CT and partial epilepsy of temporal, frontal or parietal origin.

Patients and methods

We studied 97 adult patients with partial epilepsy consecutively submitted to HM-PAO brain perfusion SPECT, 50 patients with CT abnormalities reported by a neurolradiologist were excluded. The clinical characteristics of the remaining 47 patients with partial epilepsy and normal CT are presented in Table 1. Carbamazepine was the most common antiepileptic drug, ingested as monotherapy by 33 patients and in combination with other drugs by 7 patients, while 3 patients were on valproate monotherapy and 4 patients ingested no antiepileptic drug at the time of the SPECT scanning.

Table 1. Clinical characteristics of the 47 epileptic patients

	All patients	Complex partial epilepsy n=17	Simple partial epilepsy n=6	Secondarily generalized epilepsy n=24
Mean age	35.7±1.8	35.8±2.6	29.7±3.9	37.2±3.0
Females/males	27/20	9/8	5/1	13/11
Duration of disease (years)	8.7±1.0	10.7±2.1	11.6±2.5	6.5±1.0
Mean number of fits during preceding month	76.3±21.0	186±47.3	24.3±9.3	11.0±4.7

Assessment of EEG recordings

Standard electroencephalography (EEG) was performed on all 47 patients using the equipment of Siemens Elema and results were reviewed by an experienced clinical neurophysiologist (TS) who had no information on the SPECT findings. The EEGs of the patients in this study were part of a larger material of epileptic and encephalitic patients and the scorer did not know which patients were involved in the present study. Based on all the EEGs of a patient, the type and location of the interictal EEG abnormality was assessed and scored on a scale of 0 to 6 (0 being normal and 6 maximally abnormal) in terms of diffuse non-specific disturbance (D), paroxysmal activity (P), and localized findings (L). The EEG electrode(s) revealing maximal abnormality using the 10–20 electrode placement system was also recorded. 2–17 (mean 4.8) EEGs were reviewed per patient. These included also video telemetry and/or ambulatory EEG and/or sleep deprivation recordings in 31 cases. The main findings in the EEG recordings are given in Table 2. The EEG findings were not different in terms of D, P, or L in the three different clinical subtypes of epilepsy as tested with the Mann-Whitney-U-test. In general, no major discordances were found in the consecutive EEG recordings, except in rare cases of EEGs with postictal slowing in which case the recordings were disregarded.

Based on the EEG findings two additional patient categories were defined: 1) the diffusely abnormal EEG category ($D = 0–2$, $L = 0–2$, and $D + L \geq 1$), and 2) the focally abnormal EEG category ($P \geq 2$ and $L \geq 2$ and $P + L \geq 5$) to test whether any type or location of SPECT abnormality would be explained by these two different EEG findings.

CT and MRI technology

Brain CT was performed using either a GE 8080 or Siemens Somatom scanners on all patients. Intravenous contrast medium was used in each case. All CTs were normal as interpreted by a neuroradiologist. MRI was done using the Siemens Magnetom(r) 1.0 T magnetic scanner in the mentioned cases.

SPECT imaging technology

SPECT imaging was done with a GE 400T rotating large field-of-view gamma camera equipped with a low-energy-all-purpose parallel hole collimator. The camera was connected to a PDP-11 computer running the Gamma-11 software. Filtered back projection algorithm using a modified Shepp-Logan filter was used for producing the tomograms. Imaging was performed by using 10.0–19.0 mCi (mean ± SD 14.7 ± 0.35 mCi) of ^{99m}Tc-labelled HM-PAO. The tracer was injected intravenously in a dimly lit room with the patient not required to close eyes. Simultaneous EEG recording was not performed. Data acquisition was started about 5 min thereafter. Transversal, coronal and sagittal tomographic slices were printed on Polaroid colour film. The lower threshold value was set at 25%.

Assessment of SPECT images

The SPECT scans were interpreted visually by two or three investigators who had no knowledge of the clinical data and the results represent concensus among these. The temporal, parietal, occipital and frontal lobes of both hemispheres, and the cerebel-

Table 2. The EEG findings of 47 epileptic patients with normal CT

	Complex partial epilepsy n=17 severity of finding							Secondarily generalized epilepsy n=24 severity of finding							Simple partial epilepsy n=6 severity of finding						
	0	1	2	3	4	5	6	0	1	2	3	4	5	6	0	1	2	3	4	5	6
D	6	8	2	1	–	–	–	–	16	7	1	–	–	–	–	4	1	1	–	–	–
P	–	3	4	4	6	–	–	–	8	4	6	5	1	–	–	–	2	2	1	1	–
L	1	1	3	4	2	6	–	–	–	3	7	6	6	2	–	–	–	1	4	–	1

The number of patients with each specified EEG finding is given. D=diffise disturbance of the background, P=paroxysms, L=localized findings, as scored according to the severity of the finding (0=normal – 6=maximally abnormal).

lar hemispheres, were inspected in each case and the finding was classified into 5 categories: slight (Fig. 1a) or marked (Fig. 2b) hypoperfusion, slight or marked hyperfusion, and normal perfusion.

Statistics

Spearman's rank correlation test was used for calculating correlations. Analysis of variance and the Newman-Keuls post hoc test, the non-parametric Kruskall-Wallis analysis of variance and the Chi-square test were used for testing differences between groups.

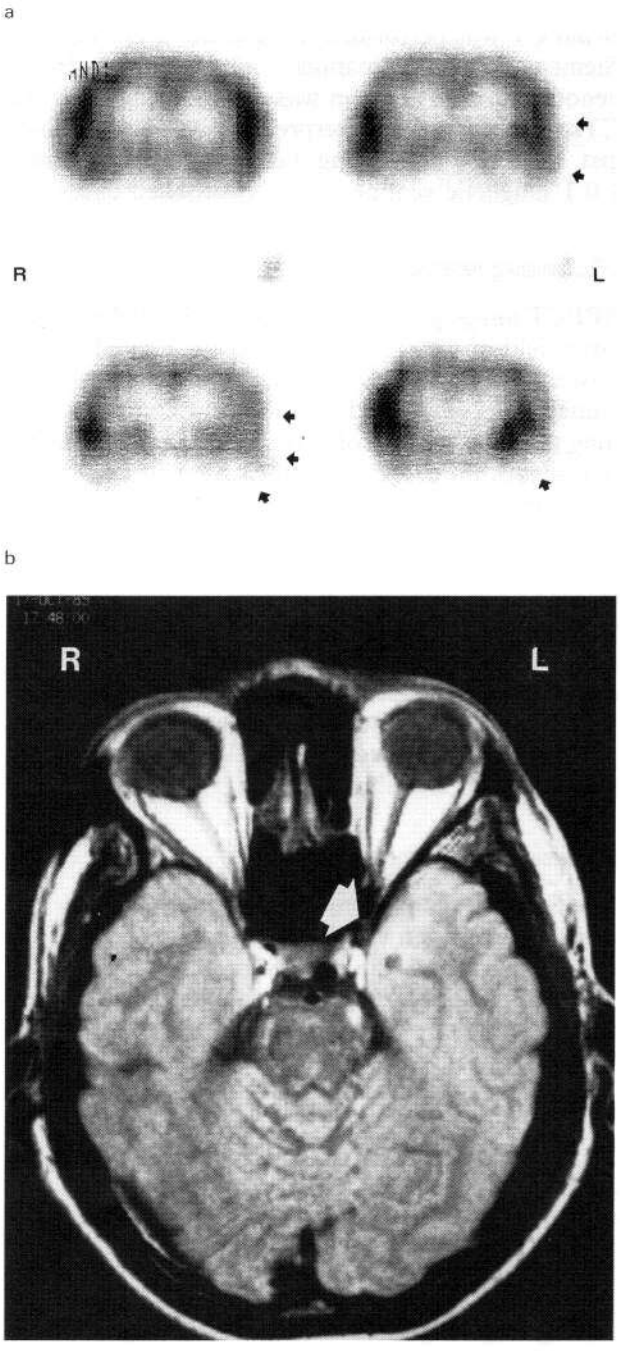

Fig. 1. a) A 46-year-old female patient with complex partial epilepsy had an EEG focus in the left temporal lobe. Hypoperfusion observed in the HM-PAO scan also was located in the left temporal lobe. b) Although CT of the head was repeatedly normal, MRI revealed a small lesion in the same area.

Results

Perfusion study results

Forty-one or 87% of the 47 patients had a hypoperfused area in SPECT and no patient had obvious hyperperfusion. The hypoperfusion was regarded as marked in 8 patients. Hypoperfusion was frontal in 19 patients and temporal in 21 patients and comprised the whole hemisphere in one case.

The relationship between hypoperfusion and EEG focus

The location of the SPECT and EEG findings are tabulated in Table 3. The hypoperfusion and the EEG focus were located in the same hemispheric lobe in 31 or 76% of the 41 patients. The frequency was about the same for both frontal (15/19 cases) and temporal (16/21 cases) foci. The hypoperfusion and the EEG focus were in the same hemisphere in 34 (83%) out of the 41 patients.

Hypoperfusion in different types of epilepsy

The severity of the hypoperfusion did not correlate with any clinical parameter and the 8 cases with a markedly hypoperfused area were distributed evenly between the three types of epilepsy. Cases illustrating slight (Fig. 1) and marked (Fig. 2) hypoperfusion are shown. Further, no particular perfusion finding was found in patients with the mainly focal, or mainly diffuse type of EEG abnormally. Hypoperfusion was

Table 3. Relationship of the location between hypoperfused areas in HM-PAO SPECT and the EEG foci in 47 patients with focal epilepsy and normal CT

	Location of the EEG focus						
	Left frontal	Left temporal	Left parietal	Right frontal	Right temporal	Right parietal	Bilateral
Location of hypoperfusion in SPECT							
Left frontal	12	–	–	2	–	–	–
Left temporal	2	12	1	1	–	–	–
Left parietal	–	–	–	–	–	–	–
Right frontal	1	1	–	3	–	–	–
Right temporal	1	–	–	–	4	–	–
Right parietal	–	–	–	–	–	–	–
Bilateral	–	–	–	–	–	–	1
Normal	2	2	–	–	1	–	1

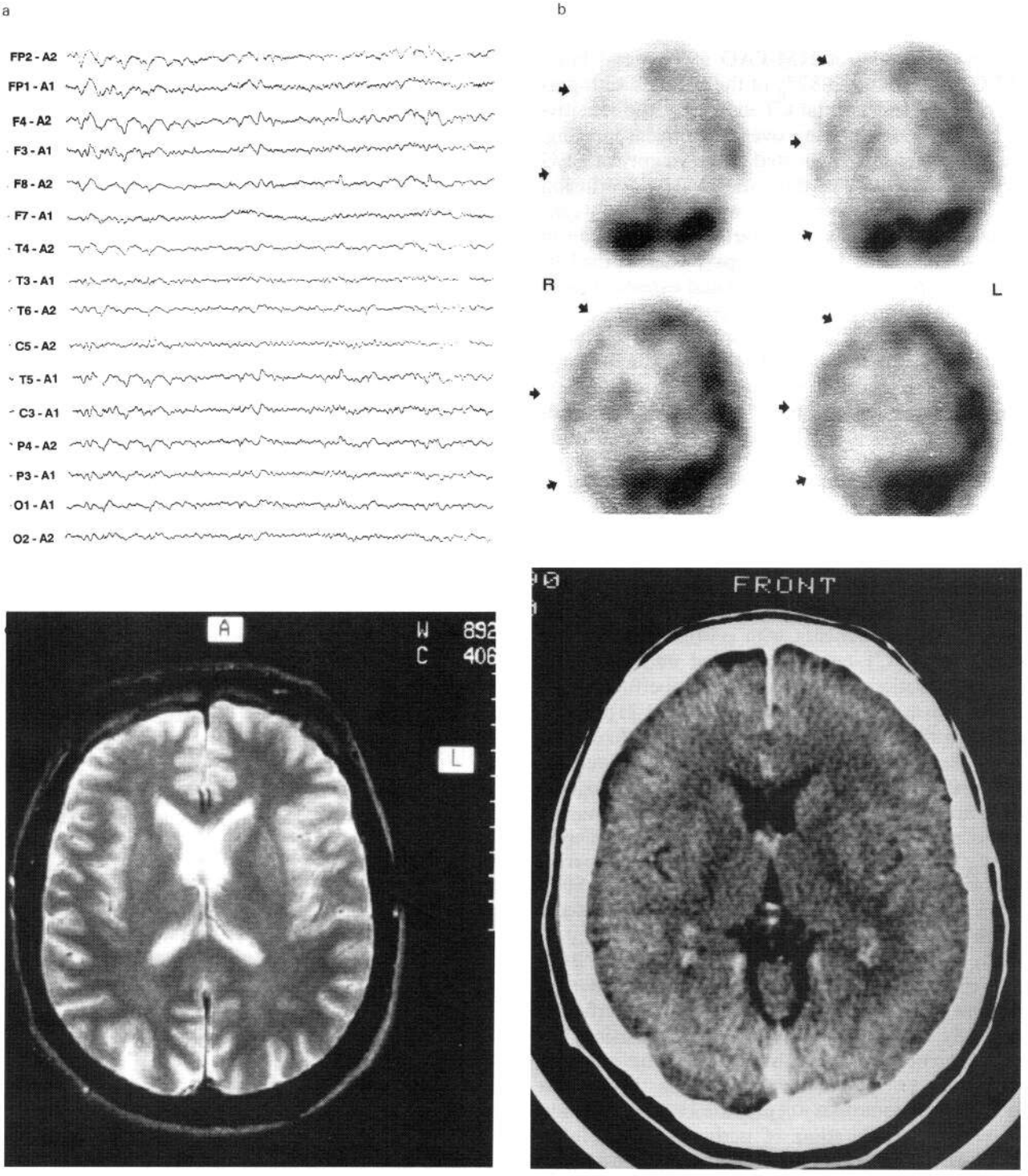

Fig. 2. a) A 45-year-old male with medically intractable complex partial seizures for 13 years had a progressing right temporal irritative focus on EEG. b) The SPECT scanning revealed a marked and wide-spread hypoperfusion in the right hemisphere in two consecutive scans two months apart. c) The follow-up with CT and d) MRI were normal. Despite of adequate antiepileptic medication the patient had daily fits.

less frequent in patients with complex partial epilepsy (12/17) than in those with simple partial (6/6) or secondarily generalized epilepsy (23/24) (Chi-square = 6.7, p = 0.035). The left-sided lateralization of hypoperfusion was more frequent in complex partial (10/12) and simple partial epilepsy (4/5) than in secondarily generalized epilepsy (16/24), but this was not statistically significant (Chi square = 1.3, p = 0.53). 5/6 of the normal scans were found in patients with complex partial epilepsy.

Discussion

Decreased uptake of HM-PAO in interictal brain SPECT was found in 87% of the patients with partial epilepsy and normal CT indicating the sensitivity of functional imaging over anatomical imaging. The rCBF defect was located in the vicinity of EEG foci in the majority of the patients. Hypoperfusion was more frequent in patients with secondarily generalized epilepsy or simple partial epilepsy than in those with complex partial epilepsy, whereas the left-sided hypoperfusion was associated especially with simple and complex partial epilepsy.

We found frontal and temporal perfusion abnormalities in equal numbers. The reason for the large number of frontal foci is unclear, but may be explained by the large number of patients with relatively severe epilepsy. Also, as the aim of this study was to clarify the value of SPECT in clinical work we used clinical CT reports for excluding patients with CT abnormalities. It is possible that the neuroradiologists tend to overlook frontal pathology and concentrate on the temporal lobes in patients with partial epilepsy.

The results show that on the basis of the brain SPECT finding patients with partial epilepsy and normal brain CT can be classified into two main groups: 1) patients in whom the hypoperfusion and EEG focus have the same location, and 2) patients in whom the hypoperfused area has a different location than their EEG focus. In the former group the hypoperfusion probably represents the epileptogenic brain area. In the latter group ictal SPECT imaging would probably clarify the laterity of the epileptic focus. The nature of the brain SPECT hypoperfusion without any EEG focus, remains unclear. Such patients may have perfusion or metabolic defects which are not electrically active interictally (9).

The severity of the hypoperfusion seen in SPECT may change with time (10) or hypoperfusion may become persistent (7). When ictal hyperperfusion gradually changes into interictal hypoperfusion, the epileptogenic brain area may during the recovery period appear quite normal. Also, as the present SPECT technique does not provide a suitable method for routine quantitation of perfusion when using ^{99m}Tc-HM-PAO (11, 12), in clinical routine as postictally hyperperfused area may be misinterpreted as normal and the normal contralateral area as being hypoperfused. Therefore, in cases with uncertainty or contradictory findings follow-up studies should be done, possibly including imaging with 123I-oimazenil (13).

Our material included patients with good seizure control but a large number of patients had daily simple or complex partial seizures. Therefore, our material represents a population of relatively poor seizure control. The larger number of interictal hypoperfused brain areas in contrast to other studies may be due to larger number of patients with severe epilepsy in our study. In conclusion, abnormalities of regional brain uptake of HM-PAO identified by SPECT give additional information on brain pathophysiology in a large proportion of patients with partial epilepsy and normal brain CT. Future studies will reveal whether perfusion studies of this kind could be used in planning and follow-up of treatment or in the classification of epilepsies.

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