
Technetium-99m-HMPAO Brain SPECT in Medically Intractable Temporal Lobe Epilepsy: A Postoperative Evaluation

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The aim of the present study was to evaluate the predictive value of interictal single-photon emission computed tomography (SPECT) using technetium-99m-labeled hexamethyl propyleneamine oxime (HMPAO) for the outcome after temporal lobectomy in patients with complex partial seizures. Out of 40 patients, 21 underwent right-sided and 19 left-sided temporal lobectomy. EEG and CT/MRI were primarily used to select the side of surgery. SPECT results correlated with temporal lobectomy in 68% of the patients. After surgical intervention, memory function was tested for both sides. Following left-sided temporal lobectomy, verbal memory was impaired in 8% of the patients, if SPECT agreed with the side selected for surgery, but in 83%, if it diverged from it. In the present study, there was no relationship between SPECT concordance with the side of temporal lobectomy and outcome as to seizure frequency and non-verbal memory. We conclude that preoperative interictal HMPAO/SPECT can contribute to the prediction of postoperative verbal memory function and that this method should be considered for use prior to temporal lobectomy.

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The controversial role of single-photon emission computed tomography (SPECT) using cerebral blood flow markers in the presurgical evaluation of patients with intractable complex partial seizures has been discussed (1-3). Extension of temporal lobectomy to more complicated cases, [e.g., to those where no lesion is detected by computed tomography/magnetic resonance imaging (CT/MRI)] requires additional diagnostic tools to identify and evaluate the brain area that is responsible for the seizures.

The aim of our study was to determine the role of hexamethyl propyleneamine oxime (HMPAO)/SPECT

imaging in patients with temporal lobe epilepsy by evaluation of the interictal period.

Although additional SPECT studies were performed in many patients ictally, under reduced anticonvulsive medication or under hyperventilation, we included only interictal SPECT studies during rest and under normal medication in this study.

METHODS

Patients

In the present study, all patients with temporal lobectomy (performed between September 1988 and December 1989) because of intractable complex partial seizures were included who presurgically underwent brain SPECT imaging with HMPAO and who could be evaluated as to memory performance and seizure frequency prior to and one year after surgery. There were 40 right-handed patients (26 females and 14 males), with ages ranging from 8 to 48 yrs (29 ± 8 ; mean \pm s.d.). Wada tests (4) were performed in all patients with left-sided and in most of the patients with right-sided temporal lobectomy. Patients who did not reveal a clearcut dominance for language of the left hemisphere were excluded from the study. Interictal HMPAO/SPECT and neuropsychologic testing were evaluated under full medication and MRI/CT had been performed prior to surgery in all patients. In order to conclusively localize the area of major EEG pathology, all patients were evaluated by continuous closed-circuit TV/EEG scalp monitoring and, in most cases, sphenoidal electrodes. In 15 cases, an electrocorticogram was necessary to identify the focus.

The presurgically obtained neuropsychologic test results of all patients were classified as (a) normal, (b) right-sided deficit, (c) left-sided deficit, and (d) bilateral deficit. The neuropsychologic testing focussed on parameters of attention, primarily on memory performance.

SPECT Technique and Evaluation

Brain SPECT was performed 30 min after i.v. injection of 555 MBq (15 mCi) technetium-99m-HMPAO. The adult dose was scaled down by body surface area for pediatric patients. Using a rotating gamma camera (Elscint Apex) equipped with a low-energy all-purpose parallel-hole collimator during a 360° rotation, 60 frames with a 64 × 64 matrix were acquired

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within 20 min. At least 2 million counts were collected for one study. Reconstruction of transaxial slices was performed by filtered backprojection using a Hamming filter with attenuation correction. Coronal and sagittal slices were created from the transaxial slices. All slices were 12 mm (2 pixels) thick. Spatial resolution was approximately 15 mm (FWHM) in the horizontal plane. All studies were performed not earlier than 48 hr after the last seizure or corresponding EEG changes.

The tomograms were evaluated blindly by five experienced nuclear medicine physicians. The SPECT images were evaluated visually according to the clinical experience of the physicians to detect a circumscribed perfusion defect in the brain. The diagnosis was established if at least four observers agreed

in their evaluation. Otherwise the patient was excluded from the study.

Postoperative Evaluation

Pathologic findings were correlated to the presurgical SPECT results.

One year after temporal lobectomy the outcome of the patients as to seizure frequency and cognitive functions was evaluated. The patients were classified as seizure-free or not seizure-free. Memory function was tested using the Benton Visual Retention Test (BVRT) and a German adaptation of the Rey Auditory Verbal Learning Test (AVLT) as described previously (5) and was considered to be significantly impaired

TABLE 1
Preoperative Results, Pathology, and Postoperative Outcome in Patients with Complex Partial Seizures

Pat.	Preoperative results			Pathology	Postoperative outcome		
	SPECT	CT/MRI	Neuro-psychometry		Seizure frequency	Verbal	Non-verbal memory
Patients with right temporal lobectomy							
1	B	R	R	Tu	F	-	0
2	B	R	R	Tu	F	0	0
3	N	R	R	Tu	F	0	0
4	R	L	R	Gl	+	0	0
5	R	R	R	Tu	F	0	0
6	N	R	R	Gl	F	0	0
7	R	R	N	Tu	F	0	0
8	R	R	R	N	F	-	0
9	R	R	R	Gl	F	0	0
10	R	R	N	N	F	0	0
11	R	L	R	Gl	F	0	0
12	R	R	R	Tu	+	0	0
13	R	N	R	Gl	F	0	0
14	R	B	B	Gl	F	0	0
15	R	N	R	Gl	F	-	0
16	N	N	R	N	U	0	0
17	R	R	R	Tu	F	0	0
18	R	N	B	Gl	F	0	0
19	N	N	N	Gl	F	0	0
20	N	N	B	Gl	F	0	0
21	R	N	R	Gl	F	0	0
Patients with left temporal lobectomy							
22	L	L	L	N	F	0	0
23	L	N	B	N	+	0	-
24	L	N	B	N	F	0	0
25	L	L	L	Tu	F	0	0
26	L	L	L	N	+	0	0
27	R	L	B	Gl	+	-	-
28	N	L	B	Tu	+	-	0
29	L	N	L	Gl	F	0	0
30	L	L	L	Tu	F	0	0
31	L	N	L	N	+	0	0
32	N	N	L	Gl	F	-	0
33	L	R	L	Gl	+	0	0
34	L	R	L	N	+	-	0
35	L	L	L	Tu	F	0	0
36	L	N	R	N	+	0	-
37	R	N	L	Gl	F	-	0
38	B	L	B	Gl	U	0	-
39	R	R	L	N	F	-	0
40	L	R	L	Gl	F	0	0

R = right; L = left; B = bilateral; N = no lesion/defect; Tu = tumor; Gl = gliosis; F = seizure-free; + = improved seizure frequency; U = unchanged seizure frequency; - = impaired memory function; and 0 = nonimpaired memory function.

TABLE 2
Localization of the Hypoperfusion in the HMPAO/SPECT Compared with CT/MRI in Complex Partial Seizures

Lesion in the CT/MRI	Lesion in the HMPAO/SPECT				Total
	Operated side	Contralateral side	Bilateral	Normal	
Operated side	12	1	3	3	19
Contralateral side	5	1	0	0	6
Bilateral	1	0	0	0	1
Without lesion in CT/MRI	9	1	0	4	14
Total	27	3	3	7	40

according to the criteria of the standardized test systems—as soon as the changes were more than two standard deviations below the initial values. Verbal and non-verbal memory performance was tested in order to distinguish left- and right-temporal neuropsychologic deficits. The postoperative changes were compared with the correlation of presurgical HMPAO/SPECT and the side selected for temporal lobectomy using Fisher's exact test for the left- and right-side operated patients, respectively.

RESULTS

Of the 40 patients studied, 21 underwent right-sided and 19 had left-sided temporal lobectomies. Table 1 shows the results of SPECT, CT/MRI, neuropsychometry, pathology, and outcome.

Twenty-six patients (65%) showed a lesion in the

CT/MRI (Table 2). In 19 cases, the lesion was on the operated side, in 6 cases on the contralateral side, and in 1 case bilateral. Thirteen lesions were preoperatively suspected to be tumors. Fourteen patients (35%) showed no lesions with CT/MRI. In 27 cases (68%), SPECT revealed a hypoperfusion on the side selected for temporal lobectomy, in 3 cases (8%) on the contralateral side, in 3 cases (8%) bilaterally, and in 7 cases (18%) no abnormality (Figs. 1–3). The lesions were located—with one exception (frontal lobe)—in the temporal lobes. Lateral and medial lesions were found as well as affections of the whole temporal lobe without a predominance of one of these lesion types. There were no significant differences as to correlation of SPECT and operated side between those patients with lesions in CT/MRI and those without (Table 2). CT/MRI and SPECT agreed in 17 cases (43%); lesions on opposite sides were observed in 6 cases (15%).

Pathologic examination revealed brain tumors in 11 cases (Table 3). There were four oligodendrogliomas, two angiomas (one calcified), two astrocytomas, one spongioblastoma, one ganglioglioma, and one hamartoma. Eighteen patients had gliosis in the resected temporal lobe. In 11 cases no pathologic alterations could be found. Seven out of the 11 patients with histologically proven brain tumor were preoperatively suspected to have tumors. In the patients with tumors, SPECT revealed hypoperfusion on the side of the lesion in seven cases (all in concordance with CT/MRI), bilateral

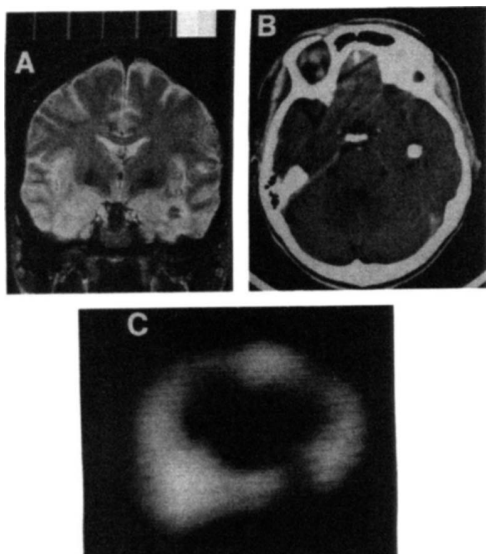


FIGURE 1

A patient with complex partial seizures. The MRI scan shows a lesion with central hypointensity and surrounding hyperintensity in the left temporal lobe (A, T2-weighted image). The lesion shows up hyperdense in the CT scan (B). The interictal HMPAO/SPECT study shows a hypoperfusion in the left temporal lobe exceeding the structural lesion (C). The right side is displayed on the viewer's left in all figures. Histology revealed an oligodendroglioma. One year after left temporal lobectomy the patient is seizure-free; verbal and non-verbal memory are unchanged (Patient 35).

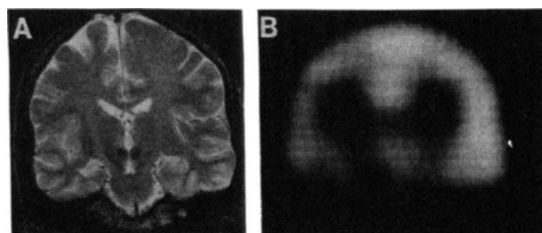


FIGURE 2

A patient with complex partial seizures. The MRI scan is normal (A, T2-weighted image). The interictal HMPAO/SPECT study shows a hypoperfusion in the right temporal lobe (B). Histology revealed a gliosis. One year after left temporal lobectomy the patient is seizure-free; verbal memory is impaired; non-verbal memory is unchanged (Patient 37).

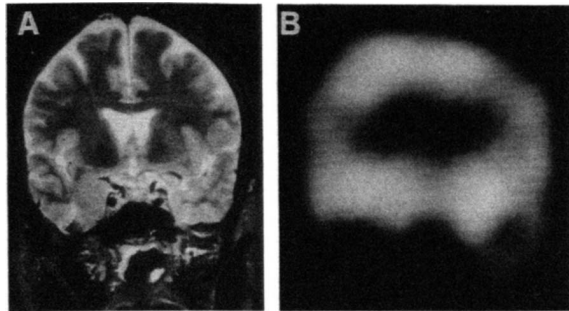


FIGURE 3
A patient with complex partial seizures. The MRI scan shows a decreased signal intensity in a circumscribed lesion in the right temporal lobe (A, T2-weighted image). The interictal HMPAO/SPECT study shows hypoperfusions in both temporal lobes (B). Histology revealed an angioma. One year after right temporal lobectomy the patient is seizure-free. Verbal memory is impaired; nonverbal memory is unchanged (Patient 1).

lesions in two cases, and a normal image in two cases. In four cases, the tumor was only diagnosed histologically. In 11 out of 18 patients with gliosis, SPECT revealed hypoperfusion on the operated side, in two cases on the contralateral side, in one case bilaterally, and in four cases a normal result (Table 3).

One year after the temporal lobectomy, 28 patients (70%) were completely seizure-free, in 10 patients (25%) seizure frequency decreased, and in 2 patients (5%) it was unchanged. Table 4 shows the distribution of these cases within the groups of patients who had left-sided and right-sided temporal lobectomy for SPECT correlation and SPECT divergence, respectively. "SPECT correlation" was assumed if the hypoperfusion in SPECT was seen solely on the side selected for temporal lobectomy. "SPECT divergence" was assumed in the remaining cases.

Thirty-one patients (78%) were unchanged/improved as to verbal memory efficiency (left temporal lobe function), but 9 (23%) were impaired postoperatively. Table 5 shows the distribution of these cases within the four groups. For the left-sided temporal lobectomy group, the correlation of SPECT agreement with the operated side and memory change is obvious. Twelve out of 13 patients with unchanged/improved

verbal memory function revealed a lesion with SPECT only on the side selected for surgery, whereas out of the six impaired cases there was only one lesion ($p < 0.01$, Fisher's exact test). Three of the remaining five patients with SPECT divergence who revealed a postoperative impaired verbal memory function had lesions on the CT/MRI scans (two on the side of temporal lobectomy and one on the side of the SPECT lesion). A brain tumor was found in one of these cases and a gliosis was found in three cases.

Thirty-six patients (90%) were unchanged/improved as to non-verbal memory (right temporal lobe function) and four (10%) were impaired. Table 6 shows the distribution of these cases within the four groups. No significant correlations could be observed.

Table 7 shows the correlation of preoperative neuropsychometry and SPECT, revealing corresponding results in 22 cases (55%).

DISCUSSION

Surgical treatment appears to be useful in patients with intractable seizures. When patients are considered candidates for surgical intervention, however, all risks associated with the procedure should be well-known and estimated as precisely as possible. Prior to surgery, all available diagnostic tools must be utilized to identify the focus. Positron emission tomography (PET) and SPECT using tracers for metabolism, blood flow, and benzodiazepin-receptors are nuclear medicine approaches that have proven useful for identification of such foci (1,6,7,8). Circumscribed ictal hyperperfusion/hypermotabolism and interictal hypoperfusion/hypometabolism represents the classic constellation for the epileptic focus, although (particularly ictally) additional regional cerebral blood flow changes occur distant from the epileptic focus (9-13). Whether such information obtained by functional brain imaging can be derived completely from the other presurgical data or whether there are additional data that can be obtained were the questions asked in the present study.

The value of the interictal SPECT before surgical intervention in epilepsy has been discussed (3,14-17). In the present study, in 68% of the cases SPECT correlated with the side selected for temporal lobectomy.

TABLE 3
Localization of the Hypoperfusion in the HMPAO/SPECT Compared with the Pathologic Finding in Complex Partial Seizures

Pathology	Lesion in the HMPAO/SPECT				Total
	Operated side	Contralateral side	Bilateral	Normal	
Tumor	7	0	2	2	11
Gliosis	11	2	1	4	18
No pathologic alteration	9	1	0	1	11
Total	27	3	3	7	40

TABLE 4
Correlation of HMPAO/SPECT and Postoperative Seizure Frequency in Complex Partial Seizures

		Seizure-free	Not seizure-free
Left temporal lobectomy	SPECT correlates with operated side	7	6
	SPECT diverges from operated side	3	3
Right temporal lobectomy	SPECT correlates with operated side	12	2
	SPECT diverges from operated side	6	1

In only 3 cases (8%) did SPECT show a hypoperfusion exclusive on the opposite side. Other authors report correlations of interictal SPECT and EEG between 28% (18) and 95% (15). Bonte et al. (3) observed abnormal SPECT studies using xenon-133 in 36 out of 74 patients with partial seizures in the absence of organic lesions. In 28 cases, localization agreed with the interictal EEG. Cordes et al. (17) reported agreement of SPECT and EEG in 20 of 47 patients with temporal lobe epilepsy.

In the present study, SPECT correlated with presurgical neuropsychometry in 55% of the cases, while in only three cases (8%) SPECT and neuropsychometry revealed singular defects on the contralateral side. A good correlation of neuropsychometry and SPECT has been reported by Devous et al. (19) for partial epilepsy and by Chiron et al. (20) for the West syndrome. Our group observed a superior correlation between SPECT and neuropsychometry compared to SPECT and interictal surface EEG (unpublished data). The complication that bitemporal defects are difficult to assess by SPECT, especially on the coronal slices which are best for studying temporal lobes in most cases, must be considered. The discrepancies of SPECT and neuropsychometry in some of the patients might be caused by different medications during the examination. All studies presented here were performed under full anticonvulsive medication, but the drugs were sometimes changed during the course of presurgical evaluation. Since different

drugs influence different parameters of cognition, which can be measured by neuropsychometry, in some cases the deficit in the neuropsychometry was probably not caused by the focus alone, but additionally by the anticonvulsive medication.

In 9 of 11 patients with brain tumors, SPECT revealed a hypoperfusion on the side of the tumor (two of these patients showed bilateral SPECT lesions), while two patients presented with a normal SPECT image. CT/MRI showed lesions in all 11 cases on the side of the tumor; seven were preoperatively suspected to be tumors. Within the group of patients with divergence of SPECT and operated side and verbal memory impairment, one patient had a tumor. SPECT showed a normal image in this case. In 12 of 18 patients with gliosis, SPECT revealed a hypoperfusion on the side of surgery (one of these showed bilateral defects), in two cases contralateral defects, and in four cases a normal result. Because there is no significant correlation between pathologic findings and SPECT results in the present study, these data suggest that the lesions seen in the SPECT image were primarily functional defects and could not be used to identify brain tumors or gliosis. Corresponding results were found by Theodore et al. (8) for PET.

Our results show that the risk of impairment of the normally left lateralized verbal memory after left temporal lobectomy can be estimated according to presurg-

TABLE 5
Correlation of HMPAO/SPECT and Postoperative Verbal Memory Performance (Left Temporal Lobe Function) in Complex Partial Seizures*

		Neuropsychology (verbal memory)	
		Unchanged/improved	Impaired
Left temporal lobectomy	SPECT correlates with operated side	12	1
	SPECT diverges from operated side	1	5
Right temporal lobectomy	SPECT correlates with operated side	12	2
	SPECT diverges from operated side	6	1

* Significant correlation proven by Fisher's exact test ($p < 0.01$).

TABLE 6
Correlation of HMPAO/SPECT and Postoperative Non-verbal Memory Performance (Right Temporal Lobe Function) in Complex Partial Seizures

		Neuropsychology (non-verbal memory)	
		Unchanged/improved	Impaired
Left temporal lobectomy	SPECT correlates with operated side	11	2
	SPECT diverges from operated side	4	2
Right temporal lobectomy	SPECT correlates with operated side	14	0
	SPECT diverges from operated side	7	0

ical interictal HMPAO/SPECT studies, depending on whether it shows solely a left-sided lesion or diverging results. For postoperative seizure-status and non-verbal memory performance, no such clearcut statement can be derived from the SPECT results of the 40 patients investigated in the present study. Theodore et al. (8) observed that neither PET nor MRI are significant prognostic factors as to postoperative seizure frequency. Only the total absence of seizures was classified as improved in the present study, because in the daily life of these patients this is the only distinct improvement. In almost all patients, seizure frequency decreased postoperatively and only two patients were unchanged. A further differentiation regarding seizure frequency is difficult because in many cases a change in postoperative medication is a consideration. The fact that blood flow imaging reflects functional deficits of the brain in addition to anatomical abnormalities (in contrast to CT/MRI) might explain the good correlation between SPECT and neuropsychometry and the predictive value for postoperative verbal memory function.

In this study, interventional SPECT procedures, e.g., studies during ictal or postictal state performed in some patients, were excluded. Our goal was to investigate the value of the interictal SPECT alone in the presurgical evaluation of complex partial seizures. Some groups tried to increase the sensitivity and accuracy of SPECT by performing additional blood flow studies under various conditions (1,9,21,22) or receptor imaging (23).

TABLE 7
Correlation of HMPAO/SPECT and Preoperative Neuropsychometry in Complex Partial Seizures

Defect in the neuropsychometry	Lesion in the HMPAO/SPECT			Normal
	Right	Left	Bilateral	
Right	10	1	2	3
Left	2	10	0	1
Bilateral	3	2	1	2
Normal	2	0	0	1

The duration of the postictal state as well as typical alterations which can be expected ictally or postictally is controversial (21,22). We observed a good differentiation between psychogenic and epileptic seizures by performing HMPAO/SPECT during the seizure (24), a higher accuracy since focus localization could not be observed in our patients. Contralateral hyperperfusions and normal scans have been ictally observed (13,25). The inclusion of data from ictal HMPAO/SPECT imaging in the present study would have prevented a clearcut statistical analysis since the conditions change and the interpretation of the results is thus difficult.

The superior spatial resolution of PET might yield more information in a few patients with epilepsy from temporal lobe origin, although this may lead to an "overinterpretation" in some cases. The present study proves that the spatial resolution of SPECT using HMPAO is sufficient to reveal significant data important for clinical patient prognosis. The lack of quantification of the results is the main disadvantage of the HMPAO/SPECT compared with PET and xenon-DSPET, since it may be difficult to distinguish hypoperfusion from hyperperfusion. This has also been observed interictally (3,26), especially in the temporal region, which is often evaluated by side-to-side comparison. A semiquantitative measurement that uses cerebellum comparison is not predictive, since the cerebellum is involved in blood flow alterations in patients suffering from epilepsy (27). With the development of iodine-labeled receptor-antagonists, another disadvantage of SPECT was eliminated (23). Further studies with larger numbers of patients are necessary to investigate the value of receptor SPECT imaging in epilepsy. Since receptor affinity is influenced by various anticonvulsive drugs, this investigation may be difficult, if performed during the presurgical evaluation of patients with complex partial seizures. Metabolic parameters, which can be measured only by PET, might reveal further information in some cases, although cerebral blood flow and metabolism are closely linked in most circumstances (28).

The data presented suggest a predictive value of

interictal HMPAO/SPECT in candidates for temporal lobectomy.

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