Visual and Quantitative Analysis of Interictal SPECT with Technetium-99m-HMPAO in Temporal Lobe Epilepsy

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Interictal ^{99m}Tc-HMPAO SPECT images were compared to ictal EEG localization in 51 patients with intractable temporal lobe epilepsy to determine their usefulness for preoperative seizure focus localization. Both quantified temporal lobe asymmetry and blinded visual detection of temporal lobe hypoperfusion were employed. Visual analysis detected ipsilateral hypoperfusion in 18 (39%) of the 46 patients with a unilateral focus and contralateral hypoperfusion in 3. None of the five patients with bitemporal foci had unilateral hypoperfusion. The positive predictive value of unilateral temporal lobe hypoperfusion was 86% (18/21). Quantified anterior temporal lobe asymmetry, greater than a previously derived normal range, correctly identified the focus in 22 (48%) but gave the wrong side in 5, resulting in a predictive value of 81%. The degree of asymmetry correlated inversely with age of seizure onset, but not with other clinical parameters, histology, or verbal and nonverbal memory. The usefulness of interictal ^{99m}Tc-HMPAO SPECT for pre-operative seizure focus localization is limited by low sensitivity when performed with a conventional rotating gamma camera. This suggests that ictal or immediate postictal imaging may be necessary for this purpose.

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Intractable focal seizures affect one per thousand of the general population (*1,2*). A conservative estimate is that over 50,000 persons in the United States would benefit from surgical treatment for intractable seizures (*1*). A large population of these patients have temporal lobe epilepsy and anterior temporal lobectomy is an effective treatment for this condition. Experienced epilepsy surgery centers obtain complete or near complete abolition of seizures in over 75% of patients undergoing this operation (*3–5*). Accurate preoperative localization of the seizure focus is essential to obtain such an outcome but the complexity of this task limits the availability of surgical treatment to a few specialist centers and small numbers of patients. Consequently, new methods of seizure focus identification are needed that are efficient and reliable and can be widely deployed.

PET can accurately identify the seizure focus in 70% of patients with intractable temporal lobe seizures by demonstrating hypometabolism and hypoperfusion in the affected temporal lobe (*6–14*). This has simplified seizure localization for many patients in centers that have access to this technology. The value of SPECT is less clear. Initial reports indicated that SPECT cerebral blood flow (CBF) imaging showed perfusion defects in most patients with focal seizures (*15–18*). However, the exact relationship of the focal hypoperfusion to the ictal EEG seizure focus was often not clearly defined or the reports were based on small numbers of patients. In addition, several reports with less promising results have appeared (*19,20*). More recently, we and several other groups have reported excellent results with ictal and early postictal SPECT for seizure focus localization (*21–26*). However, such studies require close and prolonged patient monitoring as the occurrence of complex partial seizures is unpredictable. It is therefore important to accurately define the role of interictal SPECT, a simple outpatient procedure, in the evaluation of focal epilepsy.

The aim of the present study was to determine the accuracy of seizure focus localization with interictal SPECT by studying a large group of patients with well defined temporal lobe seizure foci. Temporal lobe hypoperfusion was also correlated with age of onset and frequency of seizures, verbal and nonverbal memory performance, histopathology, and postoperative seizure control.

METHODS

Patients

All patients with refractory complex partial seizures admitted to the Austin Hospital Comprehensive Epilepsy Program for surgical evaluation over an 18-mo period were examined with SPECT. Fifty-one of these patients subsequently had temporal

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lobe seizure foci documented by ictal video-EEG studies. Their mean age was 28 yr and mean seizure frequency was 9.4 per mo. All had CT and MRI (Fonar 0.3 Telsa) performed. Temporal lobe abnormalities were apparent on the CT of 5 patients (1 tumor, 4 focal atrophy) and these were excluded from some of the subsequent analysis. Abnormalities were seen only on MRI in four patients and histology showed these lesions to be small tumors. Memory function was graded as indicative of right temporal lobe pathology (i.e., nonverbal memory deficits), left temporal lobe pathology (i.e., verbal memory deficits) or non-lateralizing, by a neuropsychologist. Forty-two patients subsequently underwent anterior temporal lobectomy and all operative specimens were examined by a neuropathologist.

Ten male volunteers with a mean age of 25 yr were studied to provide normal data. All had a normal neurologic examination and no history of neurologic illness.

SPECT Acquisition

HMPAO was obtained from Amersham International in hydrolyzed kit form (Ceretec) and was reconstituted with 550 MBq (15 mCi) of ^{99m}Tc. Intravenous administration gave a whole-body effective equivalent radiation dose of 10 mSv (1.0 rem) per study. An interictal scan was performed when patients had been seizure-free for at least 24 hr. All patients were closely observed for 5 min after injection. There was no clinical evidence of a seizure over this time in any subject. For various reasons, six patients had interictal SPECT studies repeated. The second study was used for seizure localization. Postictal studies were also obtained in all patients with a mean delay from seizure onset to injection of ^{99m}Tc-HMPAO of 4.3 ± 4.5 min (*23*).

SPECT was performed with a GE Starcam 400 AC single-head rotating gamma camera with elliptical orbit and high resolution collimator (General Electric Medical Systems). Sixty-four planar images were obtained at 30 sec per image on a 128 × 128 matrix producing approximately 40,000 counts per planar image. Butterworth prefiltering and Chang attenuation correction were performed. The resolution of this system was assessed with a Jaszczak phantom filled with a 4-MBq/100 ml solution of [^{99m}Tc]pertechnetate to approximate usual brain activity. All 12-mm diameter rods were clearly visualized with this imaging protocol.

Transaxial slices were reconstructed in a plane that ran from the base of the frontal lobe to the occipital pole on a midsaggital image. Coronal slices were reconstructed perpendicular to this plane.

SPECT Analysis

Color polaroid images that contained no means of patient identification were presented to two blinded observers. Each observer independently recorded the likely seizure focus based on the location of interictal focal hypoperfusion. The observers then reviewed together any studies on which there was disagreement and reached a consensus interpretation while still blind to EEG and clinical findings. Postictal studies were also reviewed in this manner for focal hyperperfusion and hypoperfusion by the two observers. The patterns of postictal blood flow have been described elsewhere (*23*).

Quantitative analysis was performed by a single blinded observer. Activity asymmetry and normalized activity were measured using symmetrical regions of interest (ROI) placed over the temporal lobes on a 1-cm thick slice at the midtemporal level. A 5 × 8 pixel (3.1 mm/pixel) rectangle was placed over the right mesial temporal lobe to include the area of the amygdaloid nucleus and anterior hippocampus. Rectangles (3 × 12 pixels) were placed over the anterolateral and posterolateral temporal cortex and rotated to best follow the cortical outline. The regions were then mirrored across the midline with minor lateral adjustment, if necessary, to obtain the activity in the corresponding regions of the left temporal lobe. The mean count per pixel in each ROI, and in combinations of the ROI (mesial plus anterolateral to produce a combined "anterior" ROI, and all three combined to produce a "global" ROI), were then used for quantitative analyses. These regions are shown in Figure 1. Mean ROI count was normalized, using the mean whole brain count as the reference area to allow comparison to normals. Percentage asymmetry was measured with the formula: % asymmetry = 100 × (right − left)/[(right + left)/2]. Asymmetry less than the normal range indicated a right focus, while one greater than the normal range indicated a left focus.

Subcortical perfusion asymmetry was measured in the basal ganglia, thalamus, and cerebellum. Five pixel square ROIs were placed on the relevant coronal slices (3-pixel thick) over right and left basal ganglia and thalamus. A transaxial slice at the level of the mid-cerebellum was used for placement of a 5-pixel square ROI over the right and left cerebellum.

Quantitation of absolute regional cerebral blood flow was not performed. Therefore, the terms hyperperfusion and hypoperfusion, when used in this paper, refer to relative rather than absolute changes in regional perfusion.

Determination of the Seizure Focus

The seizure focus was determined by ictal EEG studies, independent of the SPECT data. Intracerebral electrode recordings were performed in 33/51 (65%) of the patients. The remainder had clear unilateral onset of epileptiform EEG activity on surface electrodes (scalp and sphenoidal) concordant with clinical, MRI, and neuropsychological data.

Statistics

Student's t-test of paired or independent samples was used as appropriate for the comparison of two groups. One-way analysis of variance (ANOVA) was used to compare the means of multiple

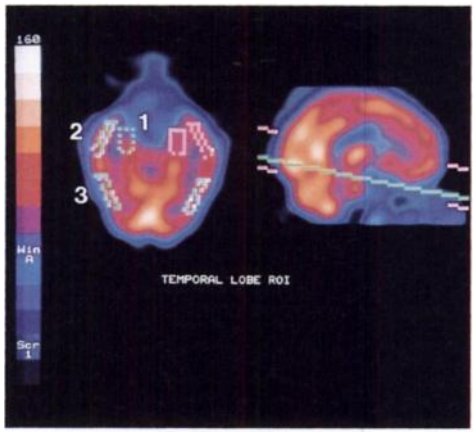

FIGURE 1. Temporal lobe ROIs used for the determination of asymmetry and normalized regional activity. 1, mesial; 2, anterolateral; 3, posterolateral. The ROI were placed on a 3-pixel thick slice at the midtemporal lobe level as shown on the sagittal image. The mean count per pixel in each ROI was used to determine the asymmetry index (A.I. = 100 × (Right − Left)/[(Right + Left)/2]).

groups. Normality of distribution and similarity of group variance was confirmed by testing plotted Nscore residuals by Filliben's method (*27*). Subsequent planned comparisons of groups was performed using the pooled estimate of variance from the ANOVA. Multiple linear regression was used to assess the effects of continuous variable data on quantified perfusion asymmetry. Chi-square was used to compare categorical data. Cohen's kappa statistic was used to compare the results of independent blinded visual analysis of the two observers (*28*).

RESULTS

Normals

Minor degrees of temporal lobe asymmetry were evident in all 10 normal subjects but not significant to mislead either observer when presented as interictal patient studies. Neither observer felt there was sufficient asymmetry to indicate a seizure focus.

The range of normal asymmetry and normalized regional activity of each of the three temporal lobe ROI were measured. The range (mean ± 2 s.d) for each region is shown in Table 1. Mesial temporal lobe asymmetry measured −10.0% to 8.1%, with similar findings for the anterolateral and posterolateral ROI. The normal range was considerably reduced by combining ROI to increase the sampling volume. The normal range of asymmetry for the anterior temporal lobe (anterolateral plus medial ROI) was −2.5% to 3.5% (sampling volume 6.8 cm^3 of each temporal lobe).

The variability in ROI placement was assessed by repeating the procedure 2 wk apart in the first five subjects. The asymmetry measurements differed by a mean of −1.5% ± 1.8% for mesial temporal lobe, −3.1% ± 5.9% for the anterolateral temporal cortex, and −0.2% ± 2.5% for the posterolateral cortex.

Visual SPECT Localization

Forty-six patients had a unilateral electrical seizure focus. Five of these patients had focal hypoperfusion corresponding to abnormalities seen on CT, one of which involved the temporal lobe contralateral to the seizure focus. When these patients were excluded, 16/41 (39%) of the remainder had unilateral temporal lobe hypoperfusion. Examples are shown in Figure 2 and results are tabulated in Table 2. In two patients, the hypoperfusion was contralateral to the focus. Two of the four patients with small temporal lobe tumors not seen on CT had normal SPECT images, while one had ipsilateral hypoperfusion and 1 had contralateral temporal lobe hypoperfusion.

Five of the 51 patients had bilateral EEG seizure foci demonstrated with intracerebral electrode studies. None had unilateral hypoperfusion. Both observers felt that visual detection of bilateral temporal lobe hypoperfusion was extremely difficult. They agreed in only two patients, both of whom had unilateral EEG foci though one has continued to have frequent seizures after surgery.

In total, 39% of the 46 patients with unilateral foci were correctly localized and 3 (6%) of all 51 patients were localized to the wrong temporal lobe by visual image analysis. These figures were obtained after a consensus review, but there was also close agreement in independent scan interpretation (observer 1: 18/46 correct, 2/46 wrong; observer 2; 23/46 correct, 4/46 wrong) with no reports in which one observer called a focus contralateral to the other observer. Cohen's kappa statistic, a measure of inter-rater agreement, was 0.73, confirming excellent agreement.

Quantitative Localization

A statistically significant difference in temporal lobe asymmetry was found between the controls and the 46 patients with normal CT scans when grouped according to seizure focus. Comparison of the mesial ($F = 9.76$, $p < 0.001$, one-way ANOVA), anterior ($F = 8.02$, $p = 0.001$), and global temporal lobe asymmetry ($F = 7.5$, $p = 0.001$), revealed highly significant differences (Table 3). However, as shown by Figure 3, the range of asymmetry overlapped considerably. Consequently, quantitative seizure focus lo-

TABLE 1
Regional Asymmetry and Normalized Activity in Normal Subjects

Region	Asymmetry index*	Normalized activity	
		Right	Left
Mesial	−1.0% ± 4.6%	1.33 ± 0.05	1.35 ± 0.04
Anterolateral	1.2% ± 4.1%	1.39 ± 0.07	1.36 ± 0.06
Posterolateral	−1.2% ± 5.2%	1.41 ± 0.10	1.45 ± 0.06
Anterior†	0.5% ± 1.5%	1.37 ± 0.05	1.36 ± 0.03
Global‡	−0.7% ± 2.0%	1.38 ± 0.06	1.39 ± 0.04

* Asymmetry index = 100 × (right − left) / [(right + left)/2] using the mean activity in each ROI. Therefore, a negative result implies relative right sided hypoperfusion while a positive result implies left hypoperfusion.

† Anterior is the mesial ROI plus the anterolateral ROI.

‡ Global is all three ROIs combined.

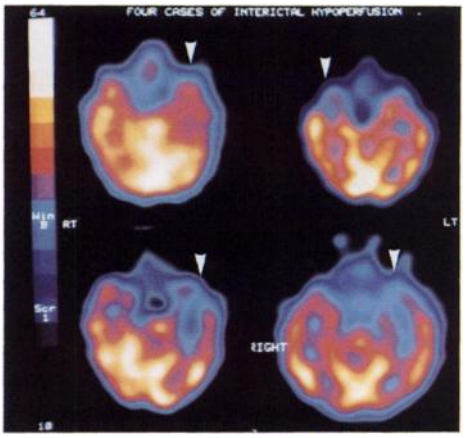

FIGURE 2. Examples of interictal unilateral temporal lobe hypoperfusion corresponding to the ictal EEG focus. The asymmetry index for each study was 11% (top left), −3% (top right), 7% (bottom left), and 10% (bottom right). (A.I. = 100 × (Right − Left)/[(Right + Left)/2].

TABLE 2
Localization by Visual Analysis of Interictal SPECT Images

EEG Focus	Unilateral = 46		Bilateral = 5
CT	Normal = 41	Abnormal = 5	Normal = 5
SPECT			
Ipsilateral	14	4	0
Contralateral	2	1	0
Bilateral	2	0	0
Normal	23	0	5

* Temporal lobe hypoperfusion relative to the seizure focus defined by ictal EEG.

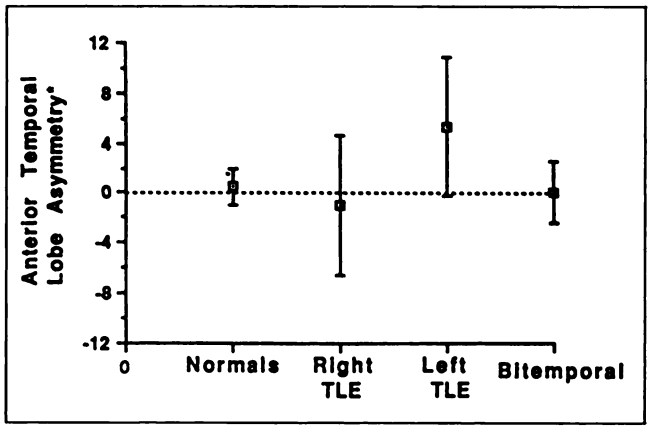

FIGURE 3. The mean and standard deviation of the anterior temporal lobe (mesial plus anterolateral ROI) asymmetry index are shown for normals, and patients with right, left and bilateral temporal lobe seizure foci. Patients with major atrophic lesions were excluded leaving 46 patients for analysis. The difference of the means was highly significant ($F = 8.02$, $p = 0.001$, one-way ANOVA), but the large overlap between the groups substantially reduced the clinical utility of this measurement.

calization by comparison of each individual's temporal lobe asymmetry to the normal range was of limited value.

The best results were obtained with anterior asymmetry (mesial ROI plus anterolateral ROI). Twenty-two (54%) of the 41 patients with unilateral foci and normal CT were outside of the normal range and 19 of these were correctly sided (46% correct, 7% incorrect). One of the five patients with bilateral foci also exceeded the normal range. Only 11 patients with unilateral foci were outside the normal range when the mesial ROI was used alone, with 9 correctly localized. If all regions were combined, 16 were correctly localized and 3 incorrectly sided.

In total, 48% of the 46 patients with a unilateral focus were correctly localized and 5 (10%) of all 51 patients were localized to the wrong temporal lobe by anterior temporal lobe asymmetry, producing a positive predictive value of 81%. Increasing or decreasing the criteria for significant asymmetry did not substantially improve these results (Table 4). Three of the five patients with asymmetry not corresponding to the seizure focus underwent temporal lobectomy on the side of the EEG focus. One had mesial temporal sclerosis on histology but only a 50% reduction in seizure frequency, and two had small tumors. Both have been seizure-free. One of the other two patients with misleading asymmetry had post-traumatic temporal lobe atrophy contralateral to the seizure focus and the other had bitemporal seizure onset on depth electrode studies.

Localization by declaring ROI with normalized activity more than 2 s.d. below the normal mean as the seizure focus, was less successful than using asymmetry. Ten patients had bilateral hypoperfusion by this criteria but only one had bilateral seizure foci. Another 11 had unilateral hypoperfusion, but 3 of these had a contralateral seizure focus. Similar results were obtained when the studies were normalized by cerebellar activity rather than whole brain mean count.

TABLE 3
Asymmetry According to Seizure Focus

	Temporal lobe region		
EEG focus*	Mesial	Anterior	Global
Right (21)	−1.4% ± 6.1%	−1.4% ± 5.6%	−1.3% ± 4.1%
Left (20)	7.1% ± 6.7%	5.3% ± 5.6%	3.7% ± 4.7%
Bilateral (5)	1.0% ± 3.8%	−0.9% ± 1.2%	0.1% ± 2.5%
Controls (10)	−1.0% ± 4.6%	0.5% ± 1.5%	−0.7% ± 2.0%

* Defined by ictal EEG. The number of subjects for each focus is shown in brackets. Patients with lesions on CT were excluded.

Variation in Interictal Temporal Lobe Perfusion

Six patients had two interictal scans. The anterior temporal lobe asymmetry of each scan is shown in Table 5. Two patients had relative hypoperfusion that changed sides between scans. The change in perfusion between studies was visually obvious and confirmed by asymmetry measurement. Both had multiple seizures the day before the first study, though none for 24 hr immediately preceding the scan. Anticonvulsant medication had been reinstated the day prior to the study. One had several auras in the hours preceding the first SPECT scan. Both had been

TABLE 4
Asymmetry Versus Sensitivity and Positive Predictive Value of Interictal SPECT Localization

Asymmetry*	Sensitivity†	Positive predictive value‡
>1 s.d.	59% (27/46)	71% (27/38)
>2 s.d.	48% (22/46)	81% (22/27)
>3 s.d.	39% (18/46)	82% (18/22)
>4 s.d.	33% (15/46)	88% (15/17)

* Degree of asymmetry expressed as greater than the number of standard deviations from the normal mean.

† Hypoperfusion on the side of the electrical focus in the 46 patients with unilateral TLE.

‡ All 51 patients included in analysis.

TABLE 5
Temporal Lobe Asymmetry with Repeated Studies in Six Patients

EEG focus	First study	Second study
Right	8.1%	−6.2%
Left	−5.8%	4.9%
Bilateral	−0.3%	−0.8%
Bilateral	−1.6%	0.8%
Right	−8.5%	−12.9%
Bilateral	−1.2%	−2.0%

TABLE 6
Histology and Imaging in 32 Patients with Adequate Tissue

Histology	Number	SPECT	CT	MRI
Normal	9	1 (11%)	1	2*
Hippocampal Sclerosis	13	7 (54%)	0	6*
Tumour	5	2 (40%)	1	5
Dysplasia	5	3 (60%)	1	1

* Probable hippocampal sclerosis.

on their usual anticonvulsant medication and free of seizures and auras for at least 48 hr at the time of the second study. In both cases, the initial study showed relative hypoperfusion contralateral to the seizure focus.

Correlation of Asymmetry with Clinical Parameters and Histology

A weak inverse correlation was found between the age of onset of seizures and the magnitude of temporal lobe hypoperfusion measured by asymmetry (Pearson r = −0.4), indicating that greater hypoperfusion was found in patients with an early age of onset. Patients with large atrophic lesions or bilateral foci were not included in this analysis. Linear regression showed this to be the only significant variable ($p = 0.04$) when the effects of current age, seizure frequency, and age of onset were analyzed (asymmetry = $-7.6 + 0.09 \times$ AGE $- 0.07 \times$ FREQUENCY $+ 0.24 \times$ AGE OF ONSET: $R^2 = 18.2\%$, ANOVA $p = 0.04$).

A significant difference in temporal lobe perfusion asymmetry was found between patients with verbal, nonverbal, or no memory deficits on neuropsychologic evaluation (mean perfusion asymmetry −3.1%, 3.4%, and 2.5%, respectively; $F = 4.3$, $p = 0.02$, df 2, 42: One-way ANOVA). However, when the perfusion asymmetry was compared within the group of patients with a right sided focus, no significant difference was found between those with or without a nonverbal memory deficit ($T = 1.7$, $p = 0.1$, df 17). The same was found for patients with and without a verbal memory deficit and a left focus ($T = 0.1$, $p = 0.9$, df 13).

Thirty-two of the 42 patients who subsequently underwent anterior temporal lobectomy had adequate mesial temporal tissue in the operative specimens for meaningful analysis. Table 6 shows the frequency of interictal hypoperfusion on SPECT images according to histologic findings. When present, hypoperfusion was highly predictive of underlying pathology. However, hypoperfusion was only demonstrated in 54% of proven cases of mesial temporal sclerosis. Three small low-grade tumors were not detected on SPECT images, although they were readily apparent on MRI.

Subcortical Perfusion

No significant difference in mean perfusion asymmetry could be demonstrated between patients with right foci, left foci, bitemporal foci, or control subjects, in the basal ganglia, thalamus or cerebellum when analyzed by one-way ANOVA. In addition, in those patients who exceeded the normal range of asymmetry, there was no relationship to the side of the seizure focus.

Comparison with Early Postictal Studies

In the same 51 patients, consensus blinded visual analysis of the early postictal studies by the same two observers correctly identified the seizure focus in 70% of those with a unilateral focus with a 97% (31/32) positive predictive value in comparison to ictal EEG localization. The patterns of postictal blood flow in these patients have been recently reported (*23*).

Postoperative Seizure Control

Follow-up (mean 28 mo, range 16–36) of 41 operated patients found that 30 (73%) were seizure-free, 7 (17%) were almost seizure-free, and 4 (10%) had no worthwhile improvement. Another patient has had only 6 mo follow-up. Two patients with unilateral foci had neuropsychologic contraindications to surgery and two refused surgery. Eighteen of the 42 operated patients (43%) had visually apparent temporal lobe hypoperfusion on the side of surgery. Only one of these had a poor outcome but this patient had a large hamartoma extending posterior to the resection. Two patients had contralateral hypoperfusion but both did well. The SPECT studies of the other three patients with disappointing outcomes showed bitemporal hypoperfusion in one and no abnormality in two.

Measurement of anterior temporal lobe asymmetry revealed hypoperfusion on the side of surgery in 52% (22/42) and contralateral in 3%. Two of the patients with asymmetry indicating hypoperfusion contralateral to the focus had small tumors at the focus and the other patient had only partial benefit from surgery.

DISCUSSION

The efficacy of interictal cerebral blood flow imaging with SPECT for seizure focus localization, using ^{99m}Tc-HMPAO and a single-head rotating gamma camera, was found to be substantially less than that reported in PET studies of similar patient populations. In the present study of 51 patients extensively evaluated with ictal EEG recordings from depth or sphenoidal electrodes and documented postoperative outcome, visual analysis by blinded observ-

ers, or calculation of temporal lobe asymmetry, detected relative hypoperfusion at the seizure focus in approximately 40% of patients with a unilateral focus. PET studies for multiple centers, have shown hypometabolism and hypoperfusion in the temporal lobe containing the seizure focus in 70% of patients (*6–14*). In another 10% of our patients, hypoperfusion was found contralateral to the focus or to be unilateral in patients with bilateral foci, a figure similar to PET reports (*8,10,29*). Two studies have directly compared ^{99m}Tc-HMPAO SPECT with ^{18}F-FDG PET in a total of 14 patients with temporal lobe epilepsy (*20,30*). PET demonstrated hypometabolism corresponding to the EEG focus in 13, while SPECT showed hypoperfusion in only 8.

Statistically significant hypoperfusion of the temporal lobe on the side of the seizure focus was demonstrated in the patients with normal CT scans in this study. However, the degree of hypoperfusion relative to the contralateral temporal lobe was small and substantially less than the asymmetry reported in PET studies of glucose metabolism in intractable temporal lobe epilepsy (*6,7,10,13*). Partial volume effect due to both the lower resolution of SPECT and the larger ROI used in this study may explain this discrepancy. While this is the most likely explanation for the low sensitivity of this study, it may be that perfusion imaging is not as good for the detection of the seizure focus as metabolic imaging. Metabolism and blood flow are tightly coupled under most circumstances (*31–33*), but several small PET studies (*6,34,35*) have reported better localization with ^{18}F-FDG than with the blood flow tracers $^{13}NH_3$ and ^{15}O-water, in patients studied with both. In addition, a recent report found hypoperfusion with ^{15}O-water PET in only 58% (17/29) of patients with proven unilateral temporal lobe foci (*36*). Again this may be methodologic as the resolution and signal-to-noise ratio are lower for PET CBF studies than for PET studies of glucose metabolism. Technetium-99m-HMPAO uptake and retention correlate well with regional CBF within the low to normal range, as measured with radiolabeled microspheres and ^{15}O-water PET (*37–41*). It would therefore seem unlikely that the use of HMPAO as the CBF tracer was a factor in our results.

Our sensitivity also appears inferior to earlier ^{99m}Tc-HMPAO and ^{123}I-amine SPECT studies of epilepsy. Most of these reports did not relate findings to a rigorously defined seizure focus so that the clinical significance of the perfusion abnormalities was often unclear. One exception is the recent report of interictal hypoperfusion on ^{123}I-HIPDM SPECT images corresponding to the eventual site of surgery in 73% of 34 patients, with contralateral hypoperfusion in one (*25*). Interictal studies were repeated in 50% of patients to obtain this result but the choice of tracer cannot be discounted as a reason for their greater sensitivity. This group had earlier reported considerable variation in interictal perfusion in some patients (*19*). Others have also reported fluctuation in interictal temporal lobe perfusion (*15,17,43,44*) and reported occasional patients with interictal hyperperfusion in the temporal lobe containing the seizure focus (*43–45*). We also observed a marked change in two patients with repeated studies. Neither had clinical evidence of a seizure, but EEG was not recorded at the time of tracer injection so subclinical epileptiform activity cannot be excluded as the cause.

As our data suggest an inability to detect small reductions in regional CBF with SPECT, the lack of correlation of hypoperfusion with clinical parameters and histology is not surprising. The presence of hypoperfusion did not clearly correlate with the presence of a lateralized memory deficit nor did it correlate well with histological findings. The latter contrasts to PET studies that have shown a correlation between hypometabolism and the degree of mesial temporal sclerosis (*42*). A greater degree of relative hypoperfusion at the focus was found in those whose seizures began at an early age, but there was no relationship to current age or seizure frequency.

CONCLUSION

Interictal SPECT is of limited value in pre-operative evaluation of patients with intractable complex partial seizures. With a sensitivity of only 40% and a predictive value of 86%, it is apparent that alternate strategies are needed to improve the performance of ^{99m}Tc-HMPAO SPECT. Multi-head and dedicated brain SPECT systems may prove more sensitive due to greater resolution and signal to noise ratio than the single-head rotating gamma camera. However, we and several other groups have shown that the sensitivity and accuracy of SPECT seizure focus localization can rival, if not surpass, PET when early postictal or ictal SPECT images are obtained (*21–26*). Although methodologically demanding, ictal injection of ^{99m}Tc-HMPAO appears necessary for SPECT to play an important role in preoperative localization and reduce the need for intracranial electrode studies.

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