

Technetium-99m-HMPAO SPECT in Partial Status Epilepticus

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In this paper we correlate the findings on ^{99m}Tc -HMPAO brain SPECT with the results of clinical examinations and electroencephalography to determine the utility of SPECT in the evaluation of patients with suspected status epilepticus. **Methods:** Thirteen patients with suspected status epilepticus underwent serial neurologic examinations, serial electroencephalograms, CT/MRI scanning and ^{99m}Tc -HMPAO SPECT. Seven patients were diagnosed with status epilepticus and six patients received other neurological diagnoses. **Results:** All patients with status epilepticus at the time of the brain SPECT scan demonstrated focal hyperperfusion on SPECT in an area concordant with that suggested by EEG. One patient with status epilepticus demonstrated a persistent area of hyperperfusion on SPECT 24 hr after the cessation of status with no evidence of breakdown in the blood-brain barrier demonstrated by ^{99m}Tc -DTPA SPECT. No patient in this study without a diagnosis of status epilepticus had focal areas of hyperperfusion on SPECT. **Conclusion:** We suggest that a ^{99m}Tc -HMPAO SPECT scan demonstrating focal hyperperfusion in a patient being evaluated for partial status epilepticus is nonspecific. Even in the absence of a structural lesion causing local breakdown in the blood-brain barrier, it may indicate either ongoing status epilepticus or recently terminated status. However, a SPECT scan demonstrating no area of focal hyperperfusion argues against the diagnosis of partial status.

Key Words: partial status epilepticus; technetium-99m; HMPAO brain SPECT; electroencephalography

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The electroencephalogram (EEG) is invaluable in excluding ongoing nonconvulsive seizures in patients with altered mental status. However, epileptic seizures do not always appear on the scalp EEG (1,2) and partial status epilepticus may be associated with many different electrographic patterns (3-9). Therefore, it is often difficult to quickly diagnose status epilepticus using only clinical and electrographic criteria (10). The goal of this preliminary study was to investigate the role of ^{99m}Tc -HMPAO (hex-

amethyl-propylene-amine-oxime) SPECT in the evaluation of patients suspected of having partial status epilepticus.

SPECT imaging with flow-dependent radiotracers has potential value in evaluating status epilepticus since it has been demonstrated that there is increased regional cerebral blood flow during partial seizures (11-14,24,27). The patterns of cerebral blood flow during status epilepticus are less well understood. Lee and Goldberg (22) demonstrated a focal hypervascular pattern on carotid angiography in five patients with status epilepticus. Franck et al. (27) used PET to study five patients with "status epilepticus," demonstrating increases in cerebral blood flow and regional metabolic activity that persisted for at least three days after the cessation of seizures. Katz (16), Tatum (18) and Bauer (21) have used SPECT and Fish (23) has used MRI to demonstrate focal areas of hyperperfusion in patients with epilepsy partialis continua. Despite these reports, there have been no systematic investigations of the use of SPECT in patients with suspected status epilepticus. We therefore studied 13 patients with suspected status epilepticus using ^{99m}Tc -HMPAO SPECT in addition to serial clinical examinations, electroencephalograms and CT/MRI scans.

METHODS

Patient Population

Ten patients with suspected status epilepticus were seen at the Hospital of the University of Pennsylvania and three were seen at the Graduate Hospital between 1990 and 1991 (Patient 2 has been reported previously by Tatum et al. (18)). The results of all clinical evaluations were evaluated retrospectively. The patient group, consisting of 10 females and 3 males, ranged in age from 13 to 82 yr (Table 1).

All patients and their EEG studies were evaluated by one of the authors (W.T. or M.S.) who also made the clinical determination of status epilepticus over serial examinations.

The authors adopted the following specific criteria for making a diagnosis of definite status epilepticus which are consistent with guidelines suggested by others (3,5):

1. Repetitive focal electrographic seizures (>3) demonstrated on EEG in a patient with an abnormal neurological examination (Patients 3, 6, 7).
2. Continuous ictal activity on initial EEG evolving over a period of days to the PLEDS PLUS (periodic lateralized epileptiform discharges accompanied by rhythmic dis-

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TABLE 1
Patient Characteristics and MRI/CT Results

| Patient no. (age/sex) | Etiology of symptoms | CT/MRI | Clinical diagnosis of status epilepticus | Clinical events | Duration of clinical event |
|--------------------------|---|--|---|---|-------------------------------|
| 1 (24/F) | Right hemiatrophy | Right cerebral hemiatrophy maximum right temporal | Yes | Twitching of the left face | Weeks |
| 2 (13/F) | Prior Hx of encephalitis | Normal | Yes | Twitching of the left face and palate | Weeks |
| 3 (81/M) | Right parietal hemorrhage (2 days) | Small right parietal hemorrhage | Yes | Twitching in the left arm | Days |
| 4 (81/F) | New right hemisphere ischemia | Old left thalamic and parassagittal infarcts (>6 mo) | Yes | Unresponsive left arm and leg twitching | 4 days |
| 5 (51/F) | ETOH, old right occipital infarct (>3 mo) | Bilateral occipital white matter high signal on T2-weighted scans | Yes | Confusion, right homonymous hemianopsia | 4 days |
| 6 (69/M) | Multiple infarcts (>2 mo) | Right parietal infarct | Yes | Left body twitching | 1 day |
| 7 (68/F) | New left parieto-occipital ischemia | Normal | Yes | Episodic right eye deviation and right face twitching confused, RHH | 4 days |
| 8 (70/F) | Old left hemisphere infarct | Large old left MCA infarct and multiple lacunes (>1 yr) | No | Twitching in right leg, R hemiparesis | 4 days |
| 9 (71/F) | Multiple lobar hemorrhages (2 yr-3 wk) | Old left parieto-temporal and new right parieto-temporal hemorrhages | No | Episodic visual hallucinations confusion | 2 wk |
| 10 (44/M) | Left parietal gunshot wound | Left parieto-occipital hypodensity | No | Left-sided focal twitching, R hemi, R homonymous | 6 days |
| 11 (82/F) | New infarct (14 days) | Left periventricular occipital infarct | No | Intermittent lethargy | Days |
| 12 (53/F) | Postictal | Mild atrophy | No | Prolonged confusion, memory loss | 5 days |
| 13 (58/F) | Birth hypoxia | Left anterior temporal hypodensity C/W old trauma | No | Increased confusion, violence, right hand twitching | Weeks |

RHH = right homonymous hemianopsia, R Hemi = right hemiparesis. The times in parentheses indicate the duration of a given abnormality from onset to the initial SPECT/EEG study.

charges) and then PLEDS (periodic lateralized epileptiform discharges) electrographic patterns as described by Reiher (15) and Treiman (3) (Patient 5).

3. A clear history of the sudden loss of consciousness accompanied by prolonged hemiclonic activity with subsequent prolonged altered mental status and serial electroencephalograms showing an evolution previously described by Reiher (15) after status epilepticus (Patient 4).
4. Witnessed episodes of repetitive stereotyped clinical seizures with clear onset, evolution and end (Patients 1, 2).

None of the patients in this study exhibited generalized tonic-clonic convulsions while hospitalized.

Seven patients were diagnosed with status epilepticus on the basis of history, serial clinical examinations and electroencephalograms (SPECT results were not used in making this determination). Six patients were eventually judged as definitely not having status epilepticus.

It should be emphasized that the diagnosis of status epilepticus was made over *serial* examinations and not necessarily at the first time that the neurologic examination and EEG were performed. In particular, Patient 2 had a complete neurologic examination and multiple EEG studies while experiencing symptoms weeks before these symptoms were attributed to status epilepticus. In

Patient 5 the initial EEG was not interpreted as showing ictal changes until a second EEG was obtained 24 hr after the first. In Patient 13 an extended, 2-hr EEG/clinical examination was necessary in order to make the clinical determination that the patient did not have status epilepticus. In many of the other patients in this study there was significant discussion about the diagnosis of status epilepticus although the initial best clinical impression agreed with that made over serial clinical and EEG studies in these cases.

Any patient with status epilepticus was excluded from this study if simultaneous SPECT and EEG studies were not available. One patient with suspected status epilepticus who had undergone serial EEG and SPECT studies was excluded from this study because no definite clinical diagnosis according to the criteria outlined above could be determined.

Electroencephalogram

Each patient underwent EEG recording at the time the radiopharmaceutical was administered for the SPECT scan to determine whether there was electrographic ictal activity at this time.

EEG electrodes were applied according to the standard international 10-20 system. All patients had scalp EEG recorded for at least 1 min before and 5 min after the injection of HMPAO. Most

patients underwent serial EEG recordings before and after SPECT and two patients had continuous video-EEG monitoring.

All EEG studies were interpreted by a board-certified electroencephalographer. The results of the EEG studies are summarized in Table 2.

SPECT

All SPECT studies were performed within 120 min of the administration of approximately 20 mCi of ^{99m}Tc -labeled HMPAO (Amersham International, Arlington Heights, IL, prepared as specified by the manufacturer). Three studies were performed on a Siemens Orbiter 3700 (Siemens Inc., Hoffman Estates, IL) single-headed gamma camera. Coronal, sagittal and transverse sections were displayed for visual analysis. Ten studies were performed on a Picker-Prism (Picker Inc., Cincinnati, OH) triple-headed rotating gamma camera. All scans collected from the Picker-Prism system were obtained over a period of 40 min using high-resolution fanbeam collimators. Projection images were obtained at three-degree angle intervals on a 128×128 matrix over 360° by rotating each head 120° . Images were reconstructed in the transaxial, coronal and sagittal planes using a Butterworth 3 0.14 pre-filter with Ramp backprojection and first-order Chang attenuation correction. The reconstructed slice thickness was 10.7 mm. Daily phantom acquisitions with the Data Spectrum Deluxe 5000 phantom (Chapel Hill, NC) were used to monitor overall system performance, reconstructed image uniformity and resolution.

All SPECT studies were reviewed by a nuclear medicine physician experienced in interpreting brain SPECT studies (A.A.). SPECT studies from a total of eight patients were available for independent review by another nuclear medicine physician (C.K.) whose impressions were in agreement with those of A.A.

Interpretation of the SPECT scans was performed qualitatively by reviewing the images on a computer screen as well as the recorded hard copy films. A study was considered abnormal if the pattern of uptake of the radiotracer differed from that noted in normal controls. An area was interpreted to show increased perfusion if the degree of uptake appeared substantially greater than that of adjacent and/or contralateral areas of the brain. Conversely, a region which showed less uptake compared to adjacent and contralateral areas was read as showing hypoperfusion. This type of subjective evaluation has proven quite accurate particularly in patients with epilepsy (12,25,20).

RESULTS

Patient Population

In the patients without status epilepticus, the clinical presentations were either prolonged or intermittent alterations in mental state (Patients 9, 11, 12 and 13) or focal arrhythmic muscle twitches (Patients 8 and 10). In the nonstatus patients presenting with altered mental states, these alterations were ascribed to either a toxic-metabolic encephalopathy or to the effect of one or more cerebral parenchymal lesions. In the nonstatus patients presenting with episodic muscle twitching (Patients 8 and 10), this twitching was clinically myoclonus rather than seizure activity. In the group of patients without status epilepticus: two had infarcts, one had multiple cerebral hemorrhages, one had a parietal gunshot wound, one had perinatal hypoxia and one demonstrated a prolonged postictal state after a single seizure.

Of the seven patients diagnosed with status epilepticus,

four were thought to have either new or old cerebral infarcts, one had a new cortical hemorrhage, one had cerebral hemiatrophy and one had a history of prior encephalitis. In three patients (#1, #2 and #3), status epilepticus was ongoing at the time of the initial SPECT study. In two patients (#6 and #7), clinical and electrographic status epilepticus had ended 1 day prior to the SPECT. In two patients diagnosed with status epilepticus (#4 and #5) we could not definitively distinguish between a prolonged postictal state following status epilepticus or continuing status at the time of the initial SPECT study using clinical/electrographic criteria.

Electroencephalogram

The EEG patterns of the seven patients with status were as follows at the time of the initial SPECT study: three exhibited the PLEDS PLUS pattern, two demonstrated focal spikes and slowing, one demonstrated intermittent focal electrographic seizures and one had a normal EEG (Fig. 1B) 24 hr after the resolution of left occipital seizures (Fig. 1A). Of the six patients without status epilepticus: two EEGs demonstrated diffuse slowing, two demonstrated focal sharp waves, one demonstrated focal slowing and one demonstrated a posteriorly dominant rhythmic activity representing a superimposition of multiple frequencies.

CT/MRI

All 13 patients underwent CT or MRI scanning as part of their evaluation. Of the seven patients with status epilepticus, two (Patients 2 and 7) had normal CT/MRI images. Abnormalities in the other status epilepticus patients consisted of: bilateral (left > right) occipital high signal areas on T2-weighted MRI scans (Patient 5), a small right parietal hemorrhage (Patient 3), a right parietal infarct (Patient 6), right cerebral hemiatrophy (Patient 1) and an old thalamic infarct (Patient 4). In three of the four patients with status epilepticus and clear focal CT/MRI abnormalities, the side of the lesion on CT/MRI agreed with the localization suggested by EEG and SPECT. In Patient 4, CT demonstrated an abnormality only on the side opposite the abnormality demonstrated on EEG, SPECT and clinical examination. The patients without status epilepticus demonstrated a similar variety of abnormalities on CT/MRI scans including a left middle cerebral artery infarct (Patient 8), multiple old and new cerebral hemorrhages (Patient 9), left parieto-occipital encephalomalacia subsequent to a gunshot wound (Patient 10), a periventricular occipital infarction (Patient 11), left temporal encephalomalacia (Patient 13) and mild atrophy (Patient 12).

SPECT

Of the seven patients diagnosed with status epilepticus, six demonstrated an area of definite focal hyperperfusion on their initial SPECT study.

All three patients with definite status epilepticus at the time of the SPECT/EEG study demonstrated focal hyperperfusion in a location concordant with the EEG abnormalities. Both patients (#4 and #5) with status epilepticus

TABLE 2
SPECT and EEG Results

| Patient no. | Time at initial study | Status epilepticus at initial study | Initial EEG | Initial SPECT | Follow-up SPECT |
|-------------|---|-------------------------------------|--|--|---|
| 1 | Weeks after onset of sx | Yes | Right temporal spikes | Right temporal-parietal hyperperfusion | — |
| 2 | Weeks after onset of sx | Yes | Right central slowing and spikes | Right centro-temporal hyperperfusion | — |
| 3 | 2 days after onset of sx | Yes | Right central focal sz | Hyperperfusion on edge of right parietal hemorrhage | DTPA study no breakdown in blood-brain barrier |
| 4 | 4 days after onset of sx | Yes vs postictal | Right occipital PLEDs Plus | Right parietal hyperperfusion | 17 days after initial study: less pronounced right hyperperfusion |
| 5 | 4 days after onset of sx | Yes vs postictal | Left occipital PLEDs Plus 3 days previous: left occipital ictal beta | Left posterior temporal, parietal and occipital hyperperfusion right parieto-occipital hypoperfusion | 6 days after initial study: left temporal hypoperfusion replacing previous area of hyperperfusion |
| 6 | 1 day after cessation of status | No | Right posterior temp PLEDs Plus 4 days previous: right post temp onset sz | Right parietal hypoperfusion surrounded by area of increased perfusion | — |
| 7 | 1 day after cessation of status | No | Normal × 24 hr during status: occipital PLEDs L occipital sz | Left occipital, cingulate, and parieto-temporal hyperperfusion | 24 hr after initial study: ^{99m} Tc-DTPA normal |
| 8 | 4 days after onset of sx | No | Diffuse slowing (theta) | Left MCA hypoperfusion | — |
| 9 | Weeks after onset of sx | No | Diffuse slow muscle artifact at onset of sx: EEG showed left occipital spikes and left central delta | Right posterior temporal and parietal hypoperfusion | — |
| 10 | 6 days after onset of sx | No | Left hemispheric delta | Left parietal and occipital hypoperfusion right cerebellar hypoperfusion | — |
| 11 | 2 days after onset of sx; 14 days after infarct | No | Left hemispheric delta and left posterior temporal sharps | Left fronto-temporal and left thalamic hypoperfusion | — |
| 12 | 5 days after onset of sx | No | Left anterior temporal spikes | Slight hypoperfusion left temporal | — |
| 13 | Weeks after onset of sx | No | Diffuse slowing (theta) alpha harmonics superimposition of rhythms | Slight left temporal hypoperfusion | — |

All SPECT scans are with ^{99m}Tc-HMPAO unless noted otherwise. All follow-up ^{99m}Tc-HMPAO SPECT scans are performed after resolution of clinical and electrographic status epilepticus. PLED = periodic lateralized epileptiform discharge and sx = presenting symptoms.

in whom we could not clinically differentiate between a prolonged postictal state and ongoing status epilepticus at the time of the SPECT/EEG study also demonstrated areas of focal hyperperfusion (our criteria for the diagnosis of status epilepticus must have been met at some time during

the patients' course and not necessarily at the time of the SPECT/EEG study). None of the patients without a clinical diagnosis of status epilepticus demonstrated focal hyperperfusion on SPECT.

In two patients (#3 and #7) with focal hyperperfusion

on ^{99m}Tc -HMPAO SPECT, Tc-DTPA SPECT studies were performed as a follow-up 24 hr after the ^{99m}Tc -HMPAO SPECT and demonstrated no breakdown in the blood-brain barrier.

One patient (#6) with status epilepticus whose clinical seizures had stopped 24 hr before the SPECT/EEG study demonstrated an area of hypoperfusion surrounded by a region of relative hyperperfusion and was not classified as having an area of definite focal hyperperfusion on SPECT. This finding may represent either breakdown in the blood-brain barrier after an infarction (demonstrated on CT) or increased flow in response to continued ictal activity not recorded on the EEG.

In one patient (#7), initial EEGs demonstrated clear, frequent focal seizures with origin in the left occipital area (Fig. 1A) and serial EEGs demonstrated no further seizures for 24 hr in conjunction with a cessation of clinical seizures (Fig. 1B). In this case, HMPAO SPECT demonstrated hyperperfusion in the left occipital area and cingulate gyrus although there was no longer clinical or electrographic evidence of seizure activity (Fig. 1C).

In two patients (#4 and #5) whose initial ^{99m}Tc -HMPAO SPECT demonstrated focal hyperperfusion, a second ^{99m}Tc -HMPAO SPECT scan was obtained. Figure 2C illustrates the initial ^{99m}Tc -HMPAO SPECT in Patient 5 showing left occipital, inferior temporal and parietal hyperperfusion (with a lesser degree of right occipital hyperperfusion) at a time when the EEG (Fig. 2B) showed a PLEDS PLUS pattern of maximum amplitude in the left occipital region. In Figure 2D, a follow-up SPECT obtained 6 days after the initial scan showed left temporal hypoperfusion while the EEG demonstrated resolution of the previous abnormalities.

DISCUSSION

Status epilepticus is a condition in which seizures occur either continuously or so frequently that patients do not return to their baseline state between seizures. Serious neurologic impairments and death are potential complications of prolonged status epilepticus, especially when the diagnosis and treatment is delayed. In nonconvulsive status epilepticus, the EEG becomes the essential tool to support the clinical suspicion. Varying electrographic changes may occur. In simple partial status, scalp changes in the EEG may be subtle or absent (1). Several different types of electroencephalographic changes that occur in partial status epilepticus have been discussed by Treiman (3) and Reiher (9). When obvious electrographic seizures are present, the clinical diagnosis of status is relatively straightforward; however, when continuous ictal EEG changes with minimal evolution or periodic patterns (e.g., PLEDS) are present, the interpretation and clinical correlation of the EEG is difficult and the diagnosis of status epilepticus may be delayed. Our study suggests that the results of ^{99m}Tc -HMPAO SPECT may aid in the diagnosis of partial status epilepticus and hence speed definitive treatment.

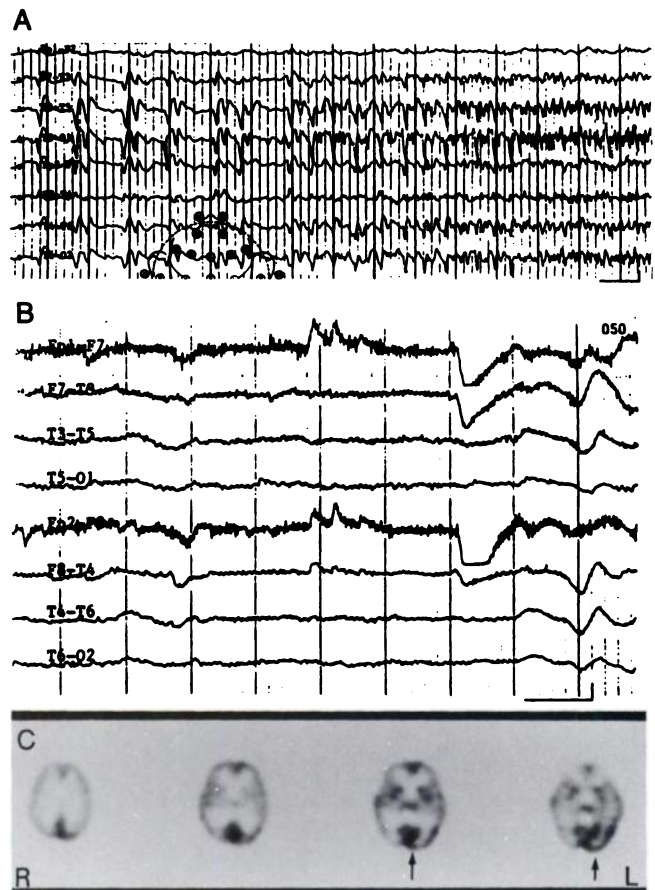


FIGURE 1. The EEGs and ^{99m}Tc -HMPAO SPECT study in Patient 7. All EEGs illustrated in this paper are presented in a longitudinal bipolar montage in which the first four channels represent an anterior-posterior left temporal chain and the second four channels represent a right anterior-posterior temporal chain. All recordings are carried out at a sensitivity of $7 \mu\text{V/mm}$ and a paper speed of 30 mm/sec. The horizontal mark in the right lower aspect of each EEG indicates 1 sec and the vertical mark in the right lower aspect of each EEG indicates an amplitude of $50 \mu\text{V}$. (A) Initial EEG showing seizures with onset in the left occipital area. (B) EEG at time of ^{99m}Tc -HMPAO SPECT demonstrating the resolution of the ictal activity seen in 1A. (C) Technetium- 99m -HMPAO SPECT performed simultaneously with the EEG tracing in 1B demonstrating left parieto-temporal, occipital, calcarine and cingulate hyperperfusion (arrows).

Of the 13 patients studied with simultaneous EEG and SPECT, seven patients were ultimately diagnosed as having status epilepticus using a combination of clinical and electrographic criteria described above. The initial clinical/electrographic impression was status epilepticus in only five of these patients. In two patients (#2 and #5), there was a delay between initial clinical/electrographic exam and the final diagnosis of status. This delay amounted to weeks in Patient 2 and 24 hr in Patient 5. Six of these patients demonstrated dramatic focal hyperperfusion on SPECT. The only patient with a diagnosis of status epilepticus in whom SPECT did not demonstrate clear focal hyperperfusion was studied more than 24 hr after the cessation of status epilepticus. All patients with clinically or electrographically defined status epilepticus at the time of

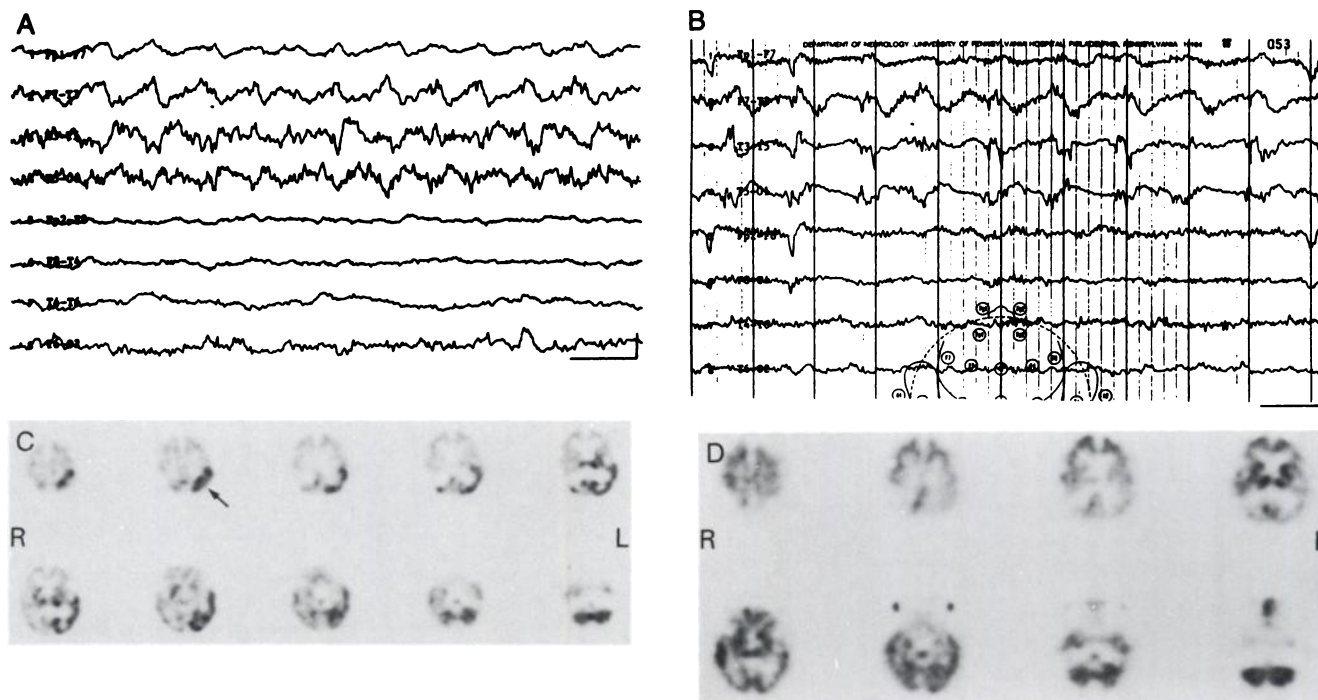


FIGURE 2. Serial EEG and ^{99m}Tc -HMPAO SPECT studies in Patient 5. (A) Initial EEG demonstrating continuous left occipital ictal beta activity superimposed on left occipital arrhythmic delta activity. (B) EEG at time of first ^{99m}Tc -HMPAO SPECT demonstrating left occipital PLEDs PLUS. (C) First ^{99m}Tc -HMPAO study showing left parietal (marked by arrow), occipital, calcarine and posterior temporal hyperperfusion, as well as right parieto-occipital hypoperfusion. A small focus of increased perfusion in the right occipital lobe is of uncertain significance. The asymmetry in the basal ganglia is due to head tilt. (D) Second ^{99m}Tc -HMPAO SPECT performed 6 days after the initial study demonstrating the resolution of the area of left-sided hyperperfusion. Both parieto-occipital areas demonstrate relative hypoperfusion.

the SPECT scan demonstrated clear areas of focal hyperperfusion. None of the six patients in whom the diagnosis of status epilepticus was considered but later disproved demonstrated areas of focal hyperperfusion on SPECT.

As in Patients 3, 4, 6 and 7, the etiology of the status epilepticus was a new structural lesion, we must consider the possibility that the focal hyperperfusion on SPECT may have been due to the acute lesion itself rather than status epilepticus. Although hyperfixation of SPECT tracers can occur as soon as 4 days after an acute infarct (28–31) (more commonly 10–14 days afterward), due to either local breakdown in the blood-brain barrier (28) or hyperemia from local tissue acidosis (29–30) which occurs in the setting of a new infarct visualizable by CT (29–31). Thus, it is unlikely that this “luxury perfusion” effect played a significant role in Patients 4 and 7 whose MRI scans did not demonstrate evidence of a structural lesion in the area where the SPECT demonstrated focal hyperperfusion. In Patients 3 and 7, DTPA-SPECT failed to demonstrate evidence of focal breakdown in the blood-brain barrier. However, in Patient 6, as CT did demonstrate a new structural lesion in the area of the hyperperfusion, we cannot eliminate the possibility that the area of hyperperfusion surrounding the area of hypoperfusion was due to “luxury perfusion.”

It is also unlikely that the areas of focal hyperperfusion seen in the SPECT studies of our patients with partial status epilepticus were due solely to motor movements as suggested by Markus (17). Focal hyperperfusion was seen

in the single patient (#5) with status who did not have focal motor movements and focal hyperperfusion was not seen in the three patients (#8, #10 and #13) who did not have status epilepticus but did have focal motor movements.

The finding of persistent focal hyperperfusion after the termination of status epilepticus in the absence of local breakdown in the blood-brain barrier is clinically important. As a result, in patients with suspected status epilepticus, the presence of focal hyperperfusion can suggest either ongoing status epilepticus or a recent history of status epilepticus. We have not determined the precise time course of this persistent hyperperfusion after status epilepticus, although in Patient 8 we observed the resolution of hyperperfusion over a period of 6 days. This finding is supported by the results of VanLandingham and Lothman (19) who demonstrated persisting hypermetabolism in an animal model of limbic status epilepticus up to 7 days after the end of status with eventual resolution within a month. On the other hand, Rowe et al. (20) have studied the patterns of regional cerebral blood flow in patients with single brief complex partial seizures and have demonstrated areas of hyperperfusion on SPECT for less than 30 min after an isolated complex partial seizure. This phenomenon was also seen in the ^{123}I -HIPDM SPECT studies of Lee et al. (13,25). The PET studies carried out by Franck (27) and Engle (14) demonstrate increased cerebral glucose utilization during seizures and, although study of the immediate ictal and postictal states with fluorodeoxyglucose (FDG) PET is limited by the long uptake period for FDG,

TABLE 3
Summary of SPECT Correlation with Clinical Diagnosis

| Clinical diagnosis | SPECT results | |
|--------------------|----------------|-------------------|
| | Hyperperfusion | No hyperperfusion |
| No status | 0 | 6 |
| Status | 6 | 1 |
| Ongoing | 3 | 0 |
| Ended | 1 | 1 |

Any patient whose SPECT scan demonstrated an area of focal hyperperfusion was placed in the first column. Any patient whose SPECT scan did not demonstrate clear focal hyperperfusion was placed in the second column. Included under the clinical diagnosis of status are all patients who had clinically determined status epilepticus at some time in their clinical course. In two patients with status, it was impossible to definitively determine whether the patient was in status at the time of the SPECT study.

inter-ictal scans in patients who do not have status epilepticus do not show areas of increased metabolic activity (32). Franck et al. (27) suggest that both this hypermetabolic state and local increases in blood flow may persist for days after the termination of status epilepticus. Thus, status epilepticus produces long-term changes in regional cerebral blood flow that are not evident after a single seizure. The etiology of this phenomenon is unclear but could be related to the accumulation of vasoactive metabolites during status or to a long-term change in functional metabolic activity (26,27). Further investigations would be required to elucidate the mechanism of this effect.

Although the number of patients in this study is small, our results suggest that ^{99m}Tc -HMPAO SPECT scanning may represent a useful adjunct in facilitating the early diagnosis of partial status epilepticus, especially in those cases where the initial EEG and clinical symptoms are difficult to interpret. An area of focal hyperperfusion is seen frequently in patients with status epilepticus occurring at some time in their clinical course and is highly sensitive for status occurring at the time of the SPECT (Table 3).

Therefore, we suggest that a SPECT scan demonstrating no area of focal hyperperfusion in a patient being evaluated for status epilepticus strongly argues against that diagnosis; however, a SPECT scan demonstrating focal hyperperfusion may indicate either ongoing status epilepticus, a history of recent status epilepticus, or "luxury perfusion" due to an acute structural lesion. Future studies with a greater number of patients will yield true measures of the specificity and sensitivity of this technique, as well as the relative discriminative power of SPECT compared with EEG studies and clinical examination. Other investigations will be required to determine whether the findings of MRI and/or Tc-DTPA SPECT studies can be used to detect those cases in which focal hyperperfusion on ^{99m}Tc -HMPAO SPECT is due to "luxury perfusion" or breakdown in the blood-brain barrier.

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EDITORIAL

The Role of SPECT Brain Imaging in Epilepsy

Seizure disorders are prevalent and serious neurological conditions (1). Long-term prognosis for patients who respond to antiepileptic drug therapy is good, with total remission expected in up to 90% of all medical responders. Unfortunately, 30%-60% of patients with complex partial seizures become medically refractory. Epilepsy surgery is considered the treatment of choice for such patients (2), and EEG monitoring is the gold standard for seizure focus localization. However, scalp EEG often fails to adequately localize the focus (3,4); depth EEG is more successful (5). Both intraoperative corticography and depth EEG are extremely invasive, expensive and present a surgical risk.

The principal motivation for functional neuroimaging in patients with refractory complex partial seizures is therefore to localize the epileptic focus. However, in this issue of *The Journal of Nuclear Medicine*, Tatum et al. (6) demonstrate a potential role for regional cerebral blood flow (rCBF) imaging by SPECT in the diagnosis of partial status epilepticus. This report provides two important reminders: First, SPECT should be used as part of a complement of diagnostic tools. Second, there can be substantial diagnostic value in a negative (normal) study. In this editorial, we examine the effectiveness of SPECT in localizing seizure foci, and highlight the ar-

eas of opportunity for SPECT imaging in epilepsy beyond focus localization.

Focus Localization in Temporal Lobe Seizures

Interictal imaging with PET and ^{18}F -fluorodeoxyglucose (FDG) demonstrates temporal lobe hypometabolism in 60%-80% of patients with complex partial seizures (7-9), but clinical utility is limited by availability and cost (9). Interictal rCBF SPECT is more accessible, but demonstrates hypoperfusion at the seizure focus with a sensitivity of only about 50% (10,11). In a recent review of SPECT in epilepsy (11), the combination of all EEG data was localizing in 71% of patients. By contrast, interictal imaging (SPECT or PET) was localizing in 59% of patients, increasing to about 90% for ictal or postictal studies (12,13).

There are three promising areas for future work regarding the role of SPECT in focus localization in partial seizures: (1) the role in postictal or ictal studies involving secondarily generalized seizures (13,14); (2) the meaning of disagreement between SPECT and EEG (some patients demonstrate focal rCBF abnormalities without EEG localization (11). Since such patients are not currently operated on, it is unknown whether the SPECT localization was correct. Other patients have normal SPECT findings in the face of localizing EEG. Devous and Leroy (15) have shown that such patients are at higher risk for poor surgical outcome than patients with localizing SPECT results); and (3) the relationship between

SPECT localization and surgical outcome. (The data described above for sensitivity of localization are relative to classical diagnostic criteria, primarily EEG. Since such criteria can be false localizing, the sensitivity of SPECT relative to surgical outcome is of greater interest.)

Extratemporal Seizures

The literature on patients with pure but extratemporal foci is sparse (16,17). Frontal lobe seizures may represent an area for concentration since they have been difficult to localize using standard EEG techniques, and depth EEG has not proven to be as beneficial for localizing the site of seizure origin as in temporal lobe seizures (18).

Primary Generalized Seizures

Little is known about abnormalities in cerebral perfusion or metabolism in generalized seizures (19-21). Using PET, Theodore et al. (19) found that interictal glucose metabolism was normal in 8/9 patients. Using SPECT, Devous et al. (20) found interictal hypoperfusion in only 3/15 patients, while Leroy et al. (21) found mild frontal rCBF abnormalities in 11/24 patients. These results are consistent with the failure of surface or depth EEG or CT and MRI to define a specific anatomic region of seizure origin in patients with absence (22).

Surgical Outcome

Most SPECT findings are compared to EEG as the gold standard in pre-surgical lesion localization. Since EEG is not infallible, SPECT should

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