4. Ward AA. Perspectives for surgical treatment of epilepsy. In: Ward AA, Penry JK, Purpura D, eds. *Epilepsy (ARNMD 61)*. New York: Raven Press; 1983:371–390.
5. Rasmussen TB. Surgical treatment of complex partial seizures: results, lessons and problems. *Epilepsia* 1983;24(suppl 1):S65–76.
6. Fisher RS, Frost JJ. Epilepsy. *J Nucl Med* 1991;32:651–659.
7. Pilcher WH, Roberts DW, Flanigan HF, et al. Complications of epilepsy surgery. In: Engel JJ, ed. *Surgical treatment of the epilepsies*. 2nd ed. New York: Raven Press; 1993:565–581.
8. Devous MDS, Leroy RF, Homan RW. Single-photon emission computed tomography in epilepsy. *Semin Nucl Med* 1990;20:325–341.
9. Shtern F. Positron emission tomography as a diagnostic tool: a reassessment based on literature review. *Invest Radiol* 1992;27:165–168.
10. Chugani HT. PET in preoperative evaluation of intractable epilepsy. *Pediatr Neurol* 1993;9:411–413.
11. Engel JJ, Henry TR, Risinger MW, et al. Presurgical evaluation for partial epilepsy: relative contributions of chronic depth-electrode recordings versus FDG-PET and scalp-sphenoidal ictal EEG. *Neurology* 1990;40:1670–1677.
12. Engel JJ, Henry TR, Risinger MW, Sutherling WW, Chugani HT. PET in relation to intracranial electrode evaluations. *Epilepsy Res Suppl* 1992;5:111–120.
13. Theodore WH, Sato S, Kufta C, Balish MB, Bromfield EB, Leiderman DB. Temporal lobectomy for uncontrolled seizures: the role of positron emission tomography. *Ann Neurol* 1992;32:789–794.
14. Chugani HT. The role of PET in childhood epilepsy. *J Child Neurol* 1994;9:S82–S88.
15. Harvey AS, Hopkins IJ, Bowe JM, Cook DJ, Shield LK, Berkovic SF. Frontal lobe epilepsy: clinical seizure characteristics and localization with ictal ^{99m}Tc-HMPAO SPECT. *Neurology* 1993;43:1966–1980.
16. Harvey AS, Bowe JM, Hopkins IJ, Shield LK, Cook DJ, Berkovic SF. Ictal ^{99m}Tc-HMPAO single-photon emission computed tomography in children with temporal lobe epilepsy. *Epilepsia* 1993;34:869–877.
17. Newton MR, Austin MC, Chan JG, McKay WJ, Rowe CC, Berkovic SF. Ictal SPECT using technetium-99m-HMPAO: methods for rapid preparation and optimal deployment of tracer during spontaneous seizures. *J Nucl Med* 1993;34:666–670.
18. Messa C, Grana C, Lucignani G, Fazio F. Functional imaging using PET and SPECT in pediatric neurology. *J Nucl Biol Med* 1994;38:85–88.
19. Spencer SS. The relative contributions of MRI, SPECT and PET imaging in epilepsy. *Epilepsia* 1994;35:S72–S89.
20. Grunwald F, Menzel C, Pavics L, et al. Ictal and interictal brain SPECT imaging in epilepsy using technetium-99m-ECD. *J Nucl Med* 1994;35:1896–1901.
21. Leveille J, Demonceau G, De RM, et al. Characterization of technetium-99m-L,L-ECD for brain perfusion imaging. Pt 2: Biodistribution and brain imaging in humans. *J Nucl Med* 1989;30:1902–1910.
22. Sharp PF, Smith FW, Gemmell HG, et al. Technetium-99m-HMPAO stereoisomers as potential agents for imaging regional cerebral blood flow: human volunteer studies. *J Nucl Med* 1986;27:171–177.
23. Marks DA, Katz A, Hoffer P, Spencer SS. Localization of extratemporal epileptic foci during ictal single-photon emission computed tomography. *Ann Neurol* 1992;31:250–255.

Evaluation of Technetium-99m-ECD in Childhood Epilepsy

Christian Menzel, Stefan Steidele, Frank Grünwald, Andreas Hufnagel, Laszlo Pavics, Christian E. Elger and Hans-J. Biersack
Departments of Nuclear Medicine and Epileptology, University of Bonn, Bonn, Germany; and Department of Nuclear Medicine, University of Szege, Szege, Hungary

In childhood epilepsy, it is difficult, but of critical importance, to determine whether surgical intervention might be beneficial for an individual patient. Because both established procedures—MRI and electroencephalography (EEG)—have limitations, interictal and ictal regional cerebral blood flow (rCBF) SPECT has proven to be a valuable adjunctive method in the presurgical evaluation of children. **Methods:** We evaluated the usefulness of the new rCBF tracer ^{99m}Tc-ECD in 14 children with focal epilepsy (mean age 9.7 yr). Eleven interictal and 8 ictal studies were performed. Results were correlated with ictal and interictal surface EEG, MRI and histological findings and the postsurgical outcome. **Results:** On the basis of the presurgical evaluation, nine patients underwent surgery. MRI studies demonstrated pathological features with possible relation to epilepsy in 50%. Overall, interictal ^{99m}Tc-ECD SPECT showed areas of hypoperfusion in 80% of patients. Ictal rCBF SPECT was informative in all patients, including one who showed bifrontal hyperperfusion in accordance with EEG results. **Conclusion:** Technetium-99m-ECD has proven to be of value for interictal and ictal rCBF SPECT in childhood epilepsy. No side effects during or after tracer administration were noticed. Ictal and interictal rCBF SPECT showed good correlation with MRI and EEG results in patients in whom correlation with the postoperative situation was possible and presented additional significant information in those patients with normal MRI and uninterpretable EEG results. No false lateralizations occurred. In children with focal epilepsy, interictal rCBF SPECT may accelerate the application of long-term electrocorticography (ECoG) in patients with normal MRI results. Ictal rCBF SPECT may also help to avoid ECoG, if a focal hyperperfusion correlates with a focal MRI abnormality, and the surface EEG gives no contradictory information.

Key Words: technetium-99m-ECD; SPECT; epilepsy; children

J Nucl Med 1996; 37:1106–1112

Received May 30, 1995; revision accepted Oct. 18, 1995.

For correspondence or reprints contact: Christian Menzel, MD, Department of Nuclear Medicine, University of Bonn, Sigmund-Freud-Strasse 25, 53105 Bonn, Germany.

Epilepsy is a common disease during childhood (*1*). Compared with epilepsy in adolescence, the variety of underlying reasons and their clinical appearance are much wider. The presurgical evaluation of many of these patients appears to be especially difficult because focal epilepsy is frequently associated with unclear symptomatology, and correlation of surface electroencephalographic (EEG) findings with regional pathology in epilepsy is difficult. Furthermore, in patients with multifocal epilepsy (e.g., Lennox-Gastaut syndrome [LGS]) (*2*), it is often difficult to identify the leading focus on the surface EEG, and MRI results are often normal in children.

In many patients with childhood epilepsy, a good prognosis can be expected. However, those children with partial seizures, especially those with multifocal epilepsy (e.g., LGS) (*3*), often have a poor prognosis for social and intellectual development because they are frequently refractory to medical treatment.

Some patients may benefit from epilepsy surgery. However, depiction of a subgroup that might benefit from surgery is more difficult in children than in adults. Although it seems logical to treat appropriate patients surgically as early as possible to allow their optimal development, it is also clinically necessary to allow some delay between the onset of an epileptic seizure and the decision to perform surgery in some cases. This is because effective and accepted investigational procedures for detection of epileptogenic foci or associated morphological abnormalities may need time to become clearly evident. For example, ictal EEG may not be able to lateralize or, if so, to provide appropriate spatial resolution if the generalization of a seizure is too fast to identify the possible origin. On this basis, it might be difficult even to distinguish between primary or secondary generalization because interictal EEG abnormalities may also be generalized or widely abandoned. Furthermore, seizure symptomatology is sometimes unclassifiable, and

TABLE 1
Clinical Data for 14 Pediatric Patients

Patient no.	Sex	Age (yr)*	Diagnosis	Type	Age at onset of epilepsy	Seizure frequency
1	M	3	Porencephaly R	SPS	2 days	4/day
2	M	8	Hamartia	CPS	2.5 yr	8/mo
3	F	13	Cavernomatosis	SPS, GM	11 yr	4–8/day
4	F	14	Focal epilepsy	SPS, CPS	5 yr	1–6/day
5	M	5.5	Hemimegalencephaly	SPS, CPS	3 mo	>50/day
6	F	13	Focal epilepsy	SPS, CPS	11 mo	>100/day
7	M	7	Lennox-Gastaut syndrome	Tonic GM, drop attack	13 mo	>50/day
8	F	13	Focal epilepsy	CPS	7 yr	50/day
9	M	17	Encephalitis	EPC	10 yr	EPC
10	M	3	Tuberous sclerosis	CPS, tonic GM	19 mo	30/mo
11	F	11	Focal epilepsy	CPS	3 yr	8/mo
12	M	5	Focal epilepsy	CPS	22 mo	20/day
13	M	8	Encephalitis	EPC	8 yr	EPC
14	M	14	Focal epilepsy	CPS, GM	13 yr	4/mo

*Age at investigation/surgery. R = right; SPS = simple partial seizures; CPS = complex partial seizures; GM = grand mal; EPC = epilepsia partialis continua.

only details obtained from the patient's history (e.g., paroxysmal hemiparesis) may yield additional information. This situation might change during the course of the disease. The MRI results may accelerate referral to surgery in a situation where clear abnormalities can be shown (*4*). However, if the morphological abnormality is either minimal or widespread, it might be difficult to detect a focal process responsible for the epilepsy. This is especially difficult during the process of brain maturation, which might be delayed in patients with epilepsy.

Fluorine-18-deoxyglucose (FDG) PET and SPECT (*5–8*) of regional cerebral blood flow (rCBF) may further be applied in children with epilepsy. The results of these studies in children with epilepsy are influenced by both functional and morphological aspects. Interictal studies do represent the sum of morphological and dysfunctional abnormalities. Ictal studies, however, mainly depict pathologically increased function and show an almost perfect correlation with EEG findings, present superior (noninvasive) spatial resolution and are interpreted best in direct correlation with interictal studies.

Given that interictal hypometabolism or hypoperfusion reflects the sum of a morphological defect and its secondary dysfunctional or inhibitory influence on surrounding areas and a consequent neuronal loss within the cortical region most affected by the seizure, it seems clear that these procedures may have a positive effect, even in patients with normal MRI results. Ictal rCBF SPECT, like EEG, is negatively influenced if seizures spread rapidly, which requires instant tracer deployment at the very beginning of the seizure. The in vitro instability of ^{99m}Tc-HMPAO has led to some difficulties in this situation. Use of ^{99m}Tc-ECD has mitigated this problem because the tracer is readily on hand, and ictal injection can be performed at the very beginning of the seizure, as required.

MATERIALS AND METHODS

Patients

We studied 14 patients (5 girls, 9 boys; age 3–17 yr; mean age 9.6 yr) who underwent interictal or ictal rCBF SPECT, or both, using ^{99m}Tc-ECD. The causes of epilepsy and clinical appearance differed widely, as did disease duration (mean duration approximately 55 mo, range 0–144 mo). Seizure frequency was relatively high (Table 1).

Electroencephalography and Long-Term Electrocorticography

All patients underwent ictal and interictal surface EEG under simultaneous video monitoring. Electrodes were applied according to the international 10/20 system and included sphenoidal electrodes in patients with suspected temporomesial seizure onset. In patients who underwent long-term electrocorticography (ECoG), strips or grids, or both, were implanted over the region of interest, partially including bitemporal hippocampal-depth electrodes. The EEG/ECoG results were interpreted according to the criteria previously described by Gloor (*9*).

MRI

All patients underwent MRI of the brain with a 1.5-T Philips Gyroscan ACS II. A standard protocol was applied, including a sagittal T1-weighted spin echo (SE) sequence, coronal and transaxial T1-weighted inversion recovery (IR) sequences, a transaxial T2-weighted and proton-weighted SE sequence and a coronal T2-weighted turbo spin echo (TSE) sequence. Depending on clinical information and the standard protocol MRI findings, most patients received additional sequences (e.g., scans before and after Gd-DTPA application) or thin (2–4 mm slice thickness) T2-weighted and proton-weighted SE coronal scans, focusing on the most probable site responsible for the epilepsy. If necessary, patients were given a tranquilizer before MRI scanning.

SPECT

Preparation of a commercially available ^{99m}Tc-ECD kit was carried out according to the manufacturer's instructions. Before injection, the radiochemical purity of the tracer was measured at >90% by thin-layer chromatography.

Tracer injections for the interictal studies were performed in the nuclear medicine department, and the administered dose was related to patient body surface (range 185–555 MBq; minimum dose 185 MBq, maximum dose 740 MBq). Interictal studies were performed without EEG control.

For the ictal studies, the tracer was injected through a prepared venous line, with the physician waiting beside the patient. The injection was done either under EEG control or immediately after the occurrence of clinical signs typical for seizure onset in the individual patient. Ictal injections were performed between 2 and

TABLE 2
Results of Electroencephalography and Ictal Electrocorticography

Patient no.	Interictal EEG results	Ictal EEG results	ECoG results
1	Hypsarrhythmia R	—	—
2	Theta-waves frontocentrotemporal L, some spikes/waves	Rhythmic delta-waves bifrontal (L > R)	Spikes, spikes/waves LF
3	Normal	Generalized depression	Spikes LF parasagittal
4	Theta-waves, sharp slow waves bifrontal	Theta-delta-waves bifrontal	—
5	Theta-waves frontocentral L	Theta-alpha-waves and triphasic waves frontocentral L	—
6	Polyspikes frontal R	Rhythmic theta-waves frontal R	—
7	Theta-delta-waves, spikes/waves frontal R	Postictal: PLEDS R	—
8	Theta-waves bitemporal L > R	Generalized theta-waves, Pct. max. frontal R spikes/waves temporal L	Spikes temporobasal-mesial L
9	EMG artifacts	—	—
10	Theta-delta-waves bifrontal and occipital L	Spikes/waves centrotemporal L	—
11	Theta-waves temporal L	Rhythmic theta-waves temporomesial L	—
12	Theta-delta-waves and spikes/waves temporal R	Rhythmic alpha-waves temporocentral L	Minimal spikes temporobasal R
13	Spikes/waves temporal L	Rhythmic theta-waves temporocentral R	—
14	Theta-arrhythmia bitemporal	—	—

EEG = electroencephalographic; ECoG = electrocorticographic; R = right; L = left; F = frontal; PLEDS = periodic lateralized epileptiform discharges.

10 sec after either EEG or clinical signs of seizure onset, and the doses were identical to those of the interictal study. If necessary, patients were given a tranquilizer before SPECT scanning but after tracer administration.

The patients were studied using an annular crystal camera. The acquisition was started no sooner than 45 min after tracer application to allow sufficient washout from extracerebral tissue. Some ictal studies were performed with a larger delay (up to 2 hr) after tracer injection. This delay was due to the time necessary for transportation of the patient from the epileptology department to the nuclear medicine department. Acquisition variables, back-projection and reconstruction followed a previously described protocol [Grünwald et al. (*10*)]. Hard copies of the scans were printed using identical thresholds in all studies. Results were evaluated using a consensus approach of three experienced readers (CM, FG, HB), who had no knowledge of the clinical information, except for the initial results of the surface EEG as to the most probable focus site.

RESULTS

Of the 14 patients evaluated in this study, 11 had simple or complex partial seizures, or both, with or without secondary generalization. Two other patients had epilepsia partialis continua, and one with LGS showed tonic grand mal seizures and sudden, short and generalized loss of muscle tone, interpreted as atonic drop attacks. On the basis of the complete presurgical evaluation, two patients had frontal lobe epilepsy; three had temporal lobe epilepsy; four had a functional affection of a

TABLE 3
Results of MRI and Interictal and Ictal Regional Cerebral Blood Flow SPECT*

Patient no.	MRI results	Interictal SPECT results	Ictal SPECT results
1	Pseudocystic destruction RH	Hypoperfusion RH	Not done
2	Abnormal gyri frontal R	Normal	Hyperperfusion frontal R
3	Cavernoma frontal parasagittal L +temporo-occipital L +frontolateral L	Not done	Frontal L (major finding)
4	Normal	Normal	Bifrontal R > L
5	Hemimegalencephaly L	Frontal L†	Frontal L
6	Disturbed gray/white matter differentiation L, atrophy R	Not done	Frontal R
7	Normal	Not done	Frontoparietal R
8	Normal	Frontotemporal L	Temporal L
9	Normal	Frontal R	Not done
10	Normal‡	Temporal L	Not done
11	Hippocampal sclerosis L	Temporal L	Not done
12	Hamartia temporal R	Bitemporal R > L	Not done
13	Normal	Temporomesial L	Not done
14	Normal	Temporomesial L	Temporomesial L§

*In general, location of pathology measured as interictal hypoperfusion or ictal hyperperfusion for regional cerebral blood flow SPECT is given.
†Indicates relative hyperperfusion due to cortical abnormality.
‡Indicates left frontocentral calcifications detected by x-ray CT.
§Indicates unchanged hypoperfusion ictally.
H = hemisphere; R = right; L = left.

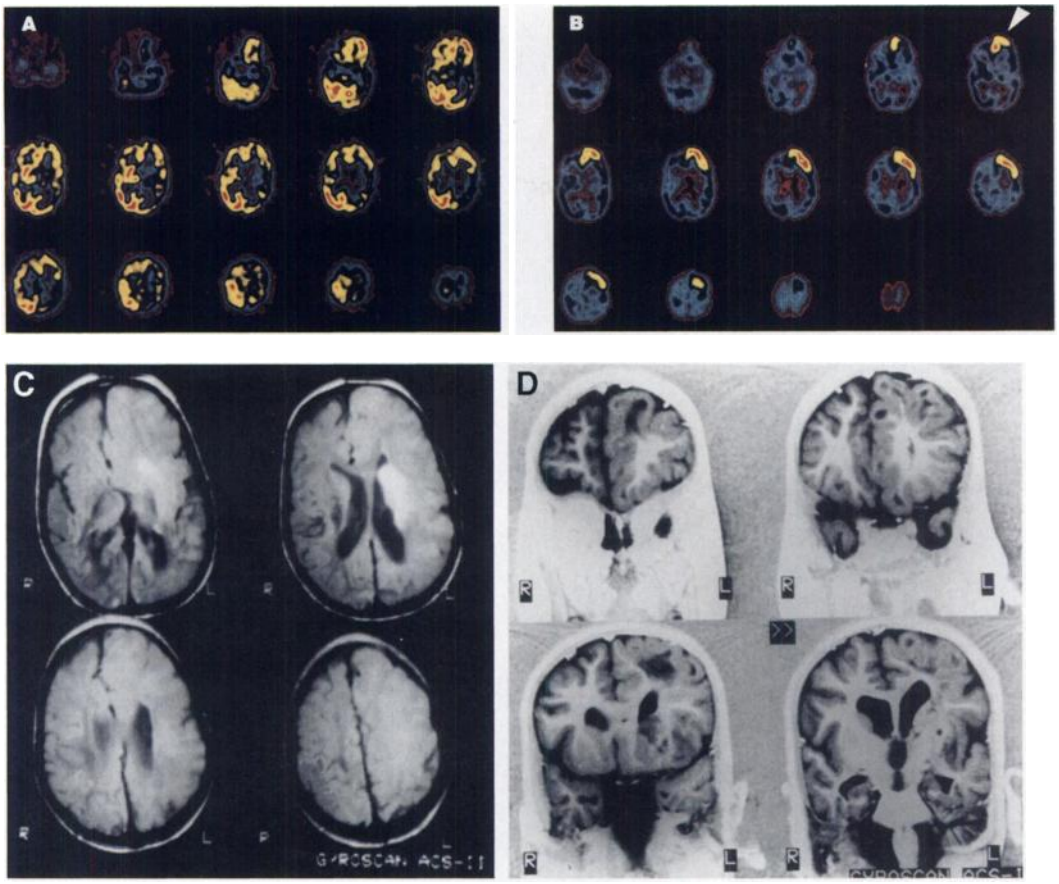

FIGURE 1. Interictal (A) and ictal (B) ^{99m}Tc-ECD SPECT in hemimegalencephaly (Patient 5), transaxial slices. Interictal study shows relatively high left frontal tracer uptake (DD: cortical thickness, subclinical seizure or prolonged increase of perfusion postictally ?) and decreased tracer uptake within the rest of the left hemisphere. Ictally, an extreme increase of cortical tracer uptake is seen within the left frontopolar region (arrowhead). MRI [transaxial rho-weighted spin echo sequence (C) and coronal TI-weighted IR sequence (D)] in this patient shows left-sided hemimegalencephaly with extreme enlargement of cortical thickness, especially within the left frontal region, and involvement of the rest of the left hemisphere, including the basal ganglia.

hemisphere that was due, respectively, to hemimegalencephaly, porencephaly, disturbed maturation and LGS. In the remaining five patients, no focus was identified at a level of confidence that allowed further evaluation or surgery (Table 1).

The surface EEG and long-term ECoG results are shown in Table 2; those for the MRI and SPECT studies are shown in Table 3. Interictal and ictal surface EEG results, correlated with MRI findings, provided sufficient information in five patients (Patients 1, 5, 6, 7 and 11) to allow surgical intervention. Only one selective surgical approach was performed without ECoG confirmation (Patient 11). Of the remaining patients, three underwent functional hemispherectomy, and one had complete callosotomy. Examples of SPECT findings are demonstrated in Figures 1–3.

Morphological abnormalities were focal in three patients, multifocal in one patient with familiar cavernomatosis (Patient 3) and showed large unilateral abnormalities or defects in three patients. MRI results were normal in the remaining seven patients, but one patient with tuberous sclerosis had discrete calcifications that were detected by x-ray CT but missed by MRI.

Interictal rCBF SPECT studies were performed in 11 of 14 patients, ictal studies in 8 of 14 and both studies in only 5. Interictal rCBF SPECT showed areas of hypoperfusion in 9 of 11 patients that corresponded to the EEG in 7 and to MRI in 4. In two patients, only structural abnormalities were detected by MRI (Patients 1 and 5). In patients with normal MRI results, interictal SPECT corresponded to the EEG at least in part in four patients (Patients 8, 10, 13 and 14). However, only one of these patients, who had matching ictal rCBF SPECT results, could undergo surgery after ECoG application (Patient 8). The other patients showed no clear EEG focus or presented multifocal abnormalities. In Patient 8, the ictal SPECT made ECoG possible; Patient 14 had nonlocalizing ictal SPECT results. No ictal SPECT was performed in the other patients. Of the remaining six patients who underwent ictal rCBF SPECT, five showed positive lateralization/detection of the affected lobe, and one had bifrontal hyperperfusion with a dominance to the right side. This patient (Patient 4) had bifrontal ictal and interictal surface EEG abnormalities. In two patients (Patients 5 and 6), the area of ictal hyperperfusion was limited to the frontopolar regions. Both patients underwent functional hemispherectomy. One of them died within 1 wk of surgery, after good initial seizure control (Table 3).

On the basis of the presurgical evaluation, 9 of 14 patients underwent surgery. Five of the nine had selective topectomy with almost total control of the seizures afterward. Three patients, each with widespread abnormalities involving large parts of a hemisphere, underwent functional hemispherectomy. The EEG showed pronounced, widespread abnormalities during ictal and interictal evaluation. Interictal SPECT in two of three patients (Patients 1 and 6) showed hypoperfusion related to known defects, and one patient (Patient 5) had relative hyperperfusion, probably due to cortical thickness in hemimegalencephaly. Ictal SPECT, performed in two of these patients (Patients 5 and 6) showed major involvement of the ipsilateral frontal lobe. Surgery was rejected for five patients because EEG results were nonlocalizing or bilateral, and MRI results were normal. All five underwent interictal SPECT, which detected focal hypoperfusion in four patients. Without additional MRI or EEG information, interictal SPECT did not lead to application of ECoG. The overall postsurgical seizure control was good (Table 4). The postsurgical follow-up period, however, is still too short to fully evaluate the surgical outcome.

Interictal rCBF SPECT detected cortical hypoperfusion in approximately 80% of patients, representing 100% with suspected temporal lobe origin and 60% with suspected frontal

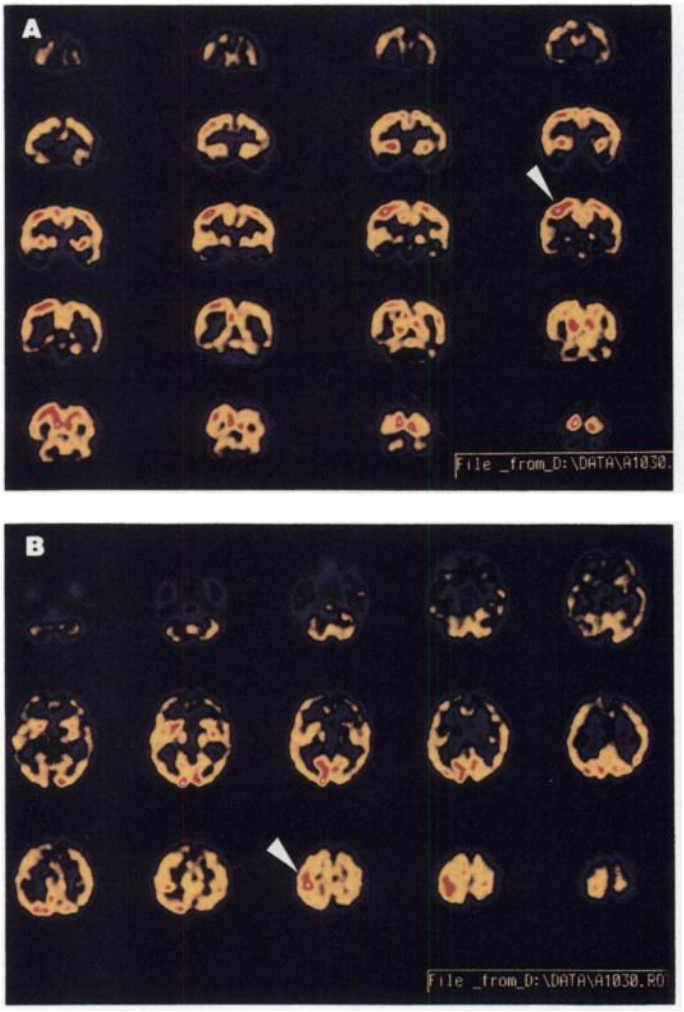

FIGURE 2. Ictal ^{99m}Tc-ECD study in Lennox-Gastaut syndrome (Patient 7): coronal (A) and transaxial (B) set of slices. A regional increase in cortical blood flow can be seen within the right frontoparietal area (arrowheads).

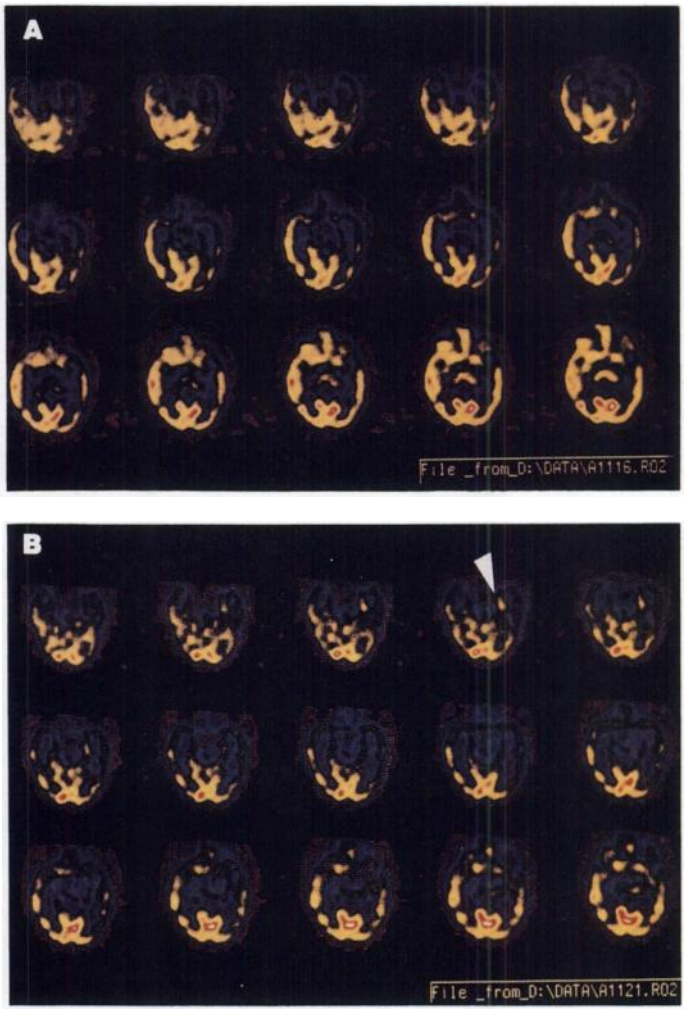

FIGURE 3. Interictal (A) and ictal (B) transaxial slices using temporal angulation (Patient 8). Interictal study shows decreased perfusion of left temporal lobe with marked reduction of rCBF within the temporomesial structures. Ictal study shows regional left temporomesial increase of rCBF (arrowhead) and widely unchanged perfusion within the rest of the left temporal lobe. The reliable interpretation of the ictal study necessitated comparison with the interictal study. MRI results in this patient were normal.

lobe origin. In those patients with postoperative confirmation of SPECT results, it appeared that all epileptogenic areas were correctly identified, but cortical hypoperfusion was usually more widespread than the site of surgery, and further areas of hypoperfusion were seen in 18% of patients. Ictal rCBF was lateralizing or detected the affected lobe in all but one patient, and these findings were consistent with those of the EEG or MRI in the patients who underwent surgery. In two patients, the ictal hyperperfusion was circumscribed and correlated well with the MRI findings. In the remaining patients, the lobe of seizure origin could be detected. In only one patient was the ictal hyperperfusion bilateral (frontal), with a right-sided dominance. Unfortunately, this patient did not undergo ECoG or surgery because the EEG also indicated a bifrontal location, and MRI results were normal.

DISCUSSION

The potential of ^{99m}Tc-ECD in medically refractory epilepsy in adults has been recently reported (*10,11*). To our knowledge, however, there are no published reports concerning its usefulness and safety in childhood epilepsy, which was the aim of the present study. Interictal rCBF SPECT using ^{99m}Tc-ECD reliably detected cortical hypoperfusion in most patients but frequently revealed relatively large areas of hypoperfusion. Ictal rCBF was lateralizing or detected the affected lobe in all but one patient, and these findings were consistent with those of the EEG or MRI in the patients who underwent surgery. In patients with focal epilepsy, the rate of detection of either interictal hypoperfusion or ictal hyperperfusion using ^{99m}Tc-ECD is moderately higher than that reported for ^{99m}Tc-HMPAO (*12*). Because of the small patient sample, however, this finding needs further evaluation. The high in vitro stability of ^{99m}Tc-ECD resulted in ictal studies that were technically easier and faster to perform than those with ^{99m}Tc-HMPAO (*13*), and it was thought that ictal studies in general were easier to perform in children than adults, mainly because of the higher seizure frequency in children. Recently, however, a method to stabilize ^{99m}Tc-HMPAO for more than 30 min has been reported (*14*).

No side effects that might have been related to ^{99m}Tc-ECD were observed. Because the morphological information derived from MRI in childhood epilepsy may be minimal, both interictal and ictal rCBF brain SPECT can contribute significantly to the presurgical evaluation of these patients. Hospitalization may also be considered stressful for children. Consequently, use of rCBF SPECT results to accelerate decision making with respect to surgery is important and might follow two routes:

1. Children with focal epilepsy and normal MRI scan results might benefit from interictal SPECT, if the latter is used to guide ECoG. Because electrode placement in temporal lobe epilepsy follows routine implantation schemes in

TABLE 4
Consequences of Presurgical Evaluation, Site of Surgical Intervention, Histological Findings and Postsurgical Situation

Patient no.	Type and site of surgery	Histological findings	Postsurgical seizure frequency	Follow-up (mo)
1	Funct. hemispherectomy R	Porencephylic cyst	Free of seizures	18
2	Lesionectomy frontal L	Ectopic neurons	Free of seizures	6
3	Lesionectomy frontal L	Cavernoma	Free of seizures	3
4	Not done			
5	Funct. hemispherectomy L	Hamartoma frontal L, marked disturbance of cortical organization	Deceased	—
6	Funct. hemispherectomy R	Disturbance of cortical organization	Free of seizures	3
7	Complete callosotomy	—	15/day	12
8	SAH L	Multiple glioneuroma hamartia	Free of seizures	6
9	Not done			
10	Not done			
11	SAH L	Ammon's horn sclerosis	1/6 mo	6
12	2/3 resection temporal R	Multiple glioneuroma hamartia	Free of seizures	3
13	Not done			
14	Not done			

Funct. = functional; R = right; L = left; SAH = selective amygdala-hippocampectomy.

many epilepsy centers, this might be of special interest in seizures of extratemporal origin. However, because ECoG in children is applied more restrictively than in adults, additional information before electrode implantation is beneficial in most cases. Nevertheless, interictal studies have limited sensitivity in children with nonlesional, focal epilepsy (*6*). A higher sensitivity for ^{18}FDG PET than rCBF SPECT has been shown in focal epilepsies in adults, and the better spatial resolution of PET is thought to be the primary reason because cerebral glucose utilization and cerebral blood flow have been shown to be closely linked (*8*). The recent development of high-resolution, dedicated brain SPECT systems has helped to increase sensitivity such that the difference in costs of both procedures may now become a more important factor. In addition, in adults false lateralization has been described in up to 10% of temporal lobe epilepsies using interictal ^{99m}Tc-HM-PAO SPECT (*13*). However, two aspects need to be considered for final evaluation of this phenomenon. Responsibility of bitemporal epileptogenic activity for "false lateralization" must be ruled out. Furthermore, the presence of subclinical epileptogenic activity or a persistent postictal hyperperfusion, both leading to a relative hyperperfusion ipsilateral to the side of the epileptogenic focus, but possibly interpreted as contralateral hypoperfusion, may bear some responsibility for the phenomenon. Quantification is one of the advantages of PET. In patients with normal MRI and nonlocalizing EEG results, this ability may be important. When utilizing ^{18}FDG PET, however, this advantage is limited by its inability to do ictal studies routinely. Nevertheless, in these patients, ictal rCBF SPECT reliably detects the lobe of seizure origin with superior specificity if the ictal SPECT study can be correlated with an interictal study. Interictal rCBF SPECT studies may further provide predictive information on postoperative seizure frequency or memory impairment, as has been reported for ^{18}FDG PET (*15*) and ^{99m}Tc-HMPAO SPECT (*12*), but not for ^{99m}Tc-ECD SPECT so far.

2. Patients with focal abnormalities on the MRI scan do benefit from ictal rCBF SPECT if a focal hyperperfusion can be detected within the vicinity of this lesion. In this situation, the interictal study is needed to improve sensitivity because hyperperfusion might be discrete and only convincingly interpreted in relation to an interictal study. However, if this match can be established, it might spare the patient the stress of ECoG, so long as the surface EEG does not provide contradictory information. Because seizures tend to spread rapidly in children, a tracer with high in vitro stability is well suited for ictal SPECT evaluation of these patients. In agreement with previous studies of adults with temporal lobe epilepsy of mesial origin (*16*), a rapid change in hyperperfusion toward temporolateral cortical areas and away from the mesial temporal lobe was also seen in some of our patients. This underscores the importance of giving the injection within the very early ictal phase (*10,17*). A similar phenomenon, however, has not yet been seen in frontal lobe epilepsy. Nevertheless, simultaneous EEG monitoring must be performed to detect the subclinical start of a seizure and to ensure that the injection is truly ictal; this might be difficult, especially in children who often present with very short seizures. This was not done in our study in all cases. To maintain early injection within reasonable logistic demands, semiautomatic injection techniques might help to decrease the logistic demand in the future (*18*).

In the present study, five patients, all with normal MRI results, were excluded from surgery on the basis of the presurgical evaluation. For different reasons, the EEG could not detect unifocal discharges. Interictal SPECT showed areas of hypoperfusion in four of the five patients, and ictal SPECT was performed in only one. Further ictal SPECT/EEG investigation might have established a clear-cut diagnosis concerning the possible site of generation of epileptic activity.

Technetium-99m-ECD seems to act as a blood flow marker in most, but not all (*19,20*), clinical situations. It has been recently proposed that ^{99m}Tc-ECD may act in part as a metabolic marker as well (*16*). Nevertheless, the opportunity to perform the injections in well-defined situations during a seizure may lead to improved detection of an epileptogenic focus itself and may further allow a better understanding of secondary outspread or the occurrence of clinical symptoms during the evolvement and spread of a seizure.

Patients with extensive morphological or nonfocal EEG

abnormalities, or both, may be considered candidates for either hemispherectomy or callosotomy. Both interventions have proved to be successful strategies (*21*). Ictal rCBF SPECT, in particular, showed focal to lobal hyperperfusion in all our patients. On the basis of the small number of patients, this finding cannot be considered a recommendation for lobectomy as an alternative approach; however, larger study populations might show the ability of ictal SPECT to identify some patients who might also benefit from more restrictive surgery.

CONCLUSION

Technetium-99m-ECD is a valuable tool for the investigation of childhood epilepsy, and application of the tracer appears to be safe. Generally, both interictal and ictal rCBF SPECT should be performed whenever possible. In childhood epilepsy, there are two major indications for the application of rCBF SPECT if the intent is to identify only the epileptogenic area: (a) the acceleration of ECoG application in patients with normal MRI scan results or low seizure frequency, or both, to shorten the hospital period of the child; and (b) to avoid ECoG in patients with focal MRI abnormalities that match ictal hyperperfusion seen on rCBF SPECT. Furthermore, interictal ^{99m}Tc-ECD SPECT might prove helpful in estimating postsurgical clinical outcome (e.g., seizure frequency or memory impairment) (*12*).

REFERENCES

1. O'Donohue NV. *Epilepsies of childhood.* London: Butterworths; 1981.
2. Gomez MR, Klass DW. Epilepsies of infancy and childhood. *Ann Neurol* 1983;13: 113–127.
3. Niedermeyer E. The Lennox-Gastaut syndrome and its frontiers. *Clin Electroencephalogr* 1986;17:117–126.
4. Grattan-Smith JD, Harvey AS, Desmond PM, Chow CW. Hippocampal sclerosis in children with intractable temporal lobe epilepsy: detection with MR imaging. *AJR Am J Roentgenol* 1993;161:1045–1048.
5. Chugani HT, Shields WD, Shewmon DA, Olson DM, Phelps ME, Pearson WJ. Infantile spasms. I. PET identifies focal cortical dysgenesis in cryptogenic cases for surgical treatment. *Ann Neurol* 1990;27:406–413.
6. Harvey AS, Bowe JM, Hopkins IJ, Shield LK, Cook DJ, Berkovic SF. Ictal ^{99m}Tc-HMPAO single-photon emission computed tomography in children with temporal lobe epilepsy. *Epilepsia* 1993;34:869–877.
7. Adams C, Hwang PA, Gilday DL, et al. Comparison of SPECT, EEG, CT, MRI and pathology in partial epilepsy. *Pediatr Neurol* 1992;8:97–103.
8. Kuhl DE, Engel J, Phelps ME, Selin C. Epileptic patterns of local cerebral metabolism and perfusion in humans determined with emission computed tomography of ^{18}FDG and $^{13}NH_3$. *Ann Neurol* 1980;8:348–360.
9. Gloor P. *Contributions of electroencephalography and electrocorticography in the neurosurgical treatment of epilepsies.* New York: Raven Press; 1987:553–571.
10. Grünwald F, Menzel C, Pavics L, et al. Ictal and interictal brain SPECT imaging in epilepsy using technetium-99m-ECD. *J Nucl Med* 1994;35:1896–1901.
11. Menzel C, Grünwald F, Pavics L, et al. Brain single-photon emission tomography using technetium-99m-bicisate (ECD) in a case of complex partial seizure. *Eur J Nucl Med* 1994;21:1243–1246.
12. Grünwald F, Durwen HF, Bockisch A, et al. Technetium-99m-HMPAO brain SPECT in medically intractable temporal lobe epilepsy: a postoperative evaluation. *J Nucl Med* 1991;32:388–394.
13. Newton MR, Austin MC, Chan G, McKay WJ, Rowe CC, Bercovic SF. Ictal SPECT using technetium-99m-HMPAO: methods for rapid preparation and optimal deployment of tracer during spontaneous seizures. *J Nucl Med* 1993;34:666–670.
14. Weisner PS, Bower GR, Dollimore LA, Forster AM, Higley B, Storey AE. A method for stabilizing technetium-99m-exametazime prepared from a commercial kit. *Eur J Nucl Med* 1993;20:661–666.
15. Radtke RA, Hanson MW, Hoffman JM, et al. Temporal lobe hypometabolism on PET: predictor of seizure control after temporal lobectomy. *Neurology* 1993;43:1088–1092.
16. Kuikka JT, Mervaala E, Vanninen E, Kälviäinen R. Does technetium-99m-bicisate image local brain metabolism in late ictal temporal lobe epilepsy. *Eur J Nucl Med* 1994;21:1247–1251.
17. Feistel H, Schüler P, Neubauer U, Stefan H, Wolf F. Frontal lobe seizures—focus localization with ictal ^{99m}Tc-HMPAO SPECT [Abstract]. *J Nucl Med* 1993;34 (suppl):207P.
18. Alksne JF, Tecoma E, Iragui-Madoz V, et al. Development of a device to facilitate routine ictal SPECT studies. *Epilepsia* 1993;34 (suppl 6):139.
19. Leveille J, Demonceau G, Walovitch RC. Intrasubject comparison between technetium-99m-ECD and technetium-99m-HMPAO in healthy human subjects. *J Nucl Med* 1992;33:480–484.
20. Moretti JL, Defer G, Cinotti L, Cesaro P, Vingeron N, Pethe C. Comparative tomoscintigraphic study of strokes using ^{99m}Tc-ECD, ^{99m}Tc-HMPAO and ^{123}I-IMP [Abstract]. *Eur J Nucl Med* 1988;12:311.
21. Vigevano F, Bertini E, Boldrini R, et al. Hemimegalencephaly and intractable epilepsy: benefits of hemispherectomy. *Epilepsia* 1989;30:833–843.

Iodine-123-Iodobenzamide Binding in Parkinsonism: Reduction by Dopamine Agonists but Not L-Dopa

Johannes Schwarz, Wolfgang H. Oertel and Klaus Tatsch

Departments of Neurology and Nuclear Medicine, Klinikum Grosshadern, Ludwig Maximilians University and German Ministry for Research and Technology Research Program Munich "Parkinson's Disease and Other Basal Ganglia Disorders," Munich, Germany

The aim of the present study was to investigate the effect of treatment with L-Dopa or a dopamine agonist, or both, on specific striatal ^{123}I-iodobenzamide (IBZM) binding using an intraindividual longitudinal design. **Method:** We prospectively studied the effect of dopaminomimetic treatment on specific [^{123}I]IBZM binding measured by SPECT in 29 patients with a clinical diagnosis of Parkinson's disease, none of whom had previously received dopaminomimetic drugs. The patients had been selected on the basis of normal subsequent specific [^{123}I]IBZM binding, semiquantitatively calculated as the basal ganglia/frontal cortex ratio, and a positive response to the dopamine agonist apomorphine before initiation of dopaminomimetic therapy. A second ^{123}I-IBZM SPECT investigation was performed after 3–6 mo of treatment with L-Dopa or a dopamine agonist, or both. **Results:** Specific [^{123}I]IBZM binding was unchanged in 10 patients treated with L-Dopa alone. However, after treatment with a dopamine agonist there was a significant decline in specific [^{123}I]IBZM binding ($p < 0.05$). After treatment with a combination of L-Dopa and a dopamine agonist, specific [^{123}I]IBZM binding was reduced without reaching a level of significance ($p = 0.08$). **Conclusion:** Short-term treatment with a dopamine agonist but not with L-Dopa reduces specific [^{123}I]IBZM binding. Therefore, before performing an [^{123}I]IBZM SPECT scan in patients previously treated with dopaminomimetic drugs, dopamine agonists should be discontinued.

Key Words: Parkinson's disease; diagnosis; iodine-123-iodobenzamide; SPECT; L-Dopa; dopamine agonist

J Nucl Med 1996; 37:1112–1115

Iodine-123-iodobenzamine (IBZM) SPECT is a predictor of dopaminergic responsiveness in previously untreated patients with parkinsonism (*1*). This capacity may also help to differ-

Received May 18, 1995; revision accepted Aug. 18, 1995.

For correspondence or reprints contact: Johannes Schwarz, MD, Department of Neurology, University of Ulm, RKU, Oberer Eselsberg 65, 84081 Ulm, Germany.