Archives of Disease in Childhood, 1988, **63,** 1184–1188

Single photon emission computed tomography in seizure disorders

R DENAYS,* M RUBINSTEIN,† H HAM,† A PIEPSZ,† AND P NOËL*

*Departments of *Neurology and †Radioisotopes, St Peter's Hospital, Free University of Brussels, Belgium*

SUMMARY Fourteen children with various seizure disorders were studied using a cerebral blood flow tracer, ^{123}I iodoamphetamine (0·05 mCi/kg), and single photon emission computed tomography (SPECT). In the five patients with radiological lesions, SPECT showed congruent or more extensive abnormalities. Five of the nine children with a normal scan on computed tomography had abnormal SPECT studies consisting of focal hypoperfusion, diffuse hemispheric hypoperfusion, multifocal and bilateral hypoperfusion, or focal hyperperfusion. A focal lesion seen on SPECT has been found in children with tonic-clonic seizures suggesting secondarily generalised seizures. Moreover the pattern seen on SPECT seemed to be related to the clinical status. An extensive impairment found on SPECT was associated with a poor evolution in terms of intellectual performance and seizure frequency. Conversely all children with a normal result on SPECT had less than two seizures per year and normal neurological and intellectual development.

The usefulness of studies with positron emission tomography in adult epilepsy is now well established.[1–3] Both cerebral metabolism and cerebral blood flow are significantly increased during focal or generalised seizures while both are depressed in the postictal and interictal state.[2 3] The presence of the interictal abnormality is remarkable in view of the fact that neuroradiological techniques usually fail to show any structural lesions in patients who might benefit from surgical treatment.[4]

Unfortunately, facilities for positron emission tomography are not widely available and remain very expensive. New cerebral blood flow tracers which are labelled with conventional γ ray emitters have been developed and allow the use of the single photon emission computed tomographic (SPECT) devices present in most nuclear medicine departments. The major determinants of the brain distribution of these tracers are cerebral blood flow and neuronal mass.[5] Although this technique is purely semiquantitative, its low cost and convenience make it highly attractive for a widespread clinical use.

Studies performed in adults using ^{123}I iodoamphetamine and SPECT have shown similar alterations as previously described in positron emission tomography.[6] Childhood epilepsy is a complex disorder, as indicated by the clinical pleiomorphism, the variety of aetiologic factors, and the unpredictable evolutions. There are only a few available data on abnormalities of cerebral metabolism in seizure disorders.[7 8] In this report we present our initial experience of cerebral blood flow imaging using ^{123}I iodoamphetamine and SPECT in children with various seizure disorders.

Patients and methods

Fourteen children aged 2 months to 16 years were investigated after informed consent of the parents and according to a protocol accepted by our local committee for medical ethics. Nine were known and treated epileptics: three had tonic-clonic seizures, two had complex partial seizures, two suffered from Bravais-Jacksonian crisis, one from absences, and one from a Lennox-Gastaut syndrome. All were investigated interictally, from three days to eight months after the last seizure. Four children were studied from 12 hours to five days after their first tonic-clonic seizures and were free from anticonvulsant treatment. One child was seen one week before the onset of tonic-clonic seizures. The reason for the examination was severe neurological hypotonia. Clinical data are presented in table 1.

High purity ^{123}I produced by the (p,5n) reaction was used to label the iodoamphetamine. Five children (patients 5, 10, 11, 13, 14) were given

Table 1 *Clinical data*

Patient No	*Age*	*Seizures*				*Treatment*	*Results of neurological and neuropsychological examination*
		Type	*Age of onset*	*Aetiology*	*Frequency*		
1	9 years	CPS	7 years	Cerebral birth injury	1-2/week	Carbamazepine	Right hemiparesia, school difficulties
2	11 years	TCS	4 years	Cerebral birth injury	1-2/year	Sodium valproate	Left hemiparesia
3	12 years	L-G	1 year	Unknown	2-3/month	Phenytoin, sodium valproate	Mentally retarded
4	13 years	TCS	13 years	Central nervous system demyelinating process	—	—	School difficulties
5	7 years	TCS	1 year	Tuberose sclerosis	2-3/month	Sodium valproate, nitrazepam	Mentally retarded
6	8 years	CPS	7 years	Unknown	3-4/week	Carbamazepine	Mentally retarded
7	16 years	B-J	1 year	Unknown	1-2/year	Sodium valproate	Normal
8	13 years	B-J	6 years	Unknown	1/year	Sodium valproate	Normal
9	12 years	TCS	4 years	Unknown	1-2/year	Sodium valproate	Normal
10	2 years	TCS	2 years	Febrile seizure	—	—	Normal
11	2 months	TCS	2 months	Unknown	—	—	Normal
12	13 years	TCS	13 years	Unknown	—	—	Normal
13	6 years	Absences	5 years	Unknown	1/month	Sodium valproate	School difficulties
14	4 months	TCS	4 months	Central nervous system heredodegenerative disease	—	—	Severe hypotonia

CPS=Complex partial seizures; TCS=Tonic-clonic seizures; B-J=Bravais-Jacksonian seizures; L-G=Lennox-Gastaut syndrome.

pentobarbitone (Nembutal, 5 mg/kg intrarectal) one hour before the examination. Patients were placed in a quiet environment, then an intravenous line was inserted into the forearm. About three minutes later 0·05 mCi/kg of ^{123}I iodoamphetamine were administered (with a minimum of 0·5 mCi) and after another 30 minutes children were taken to the camera room. Depending upon the child's size, either the head or the whole trunk was fixed in a polystyrene vacuum cushion. All the children were perfectly quiet throughout the examination. SPECT imaging was performed using an Elscint rotating camera and a low energy, high sensitivity collimator. Data for 360° were collected using 30 second frames and 6° increments. Transaxial and coronal reconstructions were calculated after a high frequency cut off using a Hamming-Hann filter by an Apex 415 computer system. The transverse axis was reorientated along the orbitomeatal line. Slices were 2 pixels thick (17 mm). After a background subtraction of 7% of the maximum, differences of more than 12% between symmetrical regions of the brain were considered significant. Computed tomography was performed in the same week with the Siemens Somatom DRH head scanner using a standard technique.

Results

The findings on electroencephalography, computed tomography, and SPECT are summarised in table 2. A normal SPECT pattern is displayed in the figure (A).

(1) PATIENTS WITH LESIONS ON COMPUTED TOMOGRAPHY (N=5)

Two children (patients 1 and 2) who had intractable complex partial seizures and rare tonic-clonic seizures, respectively, had a large sylvian porencephalic cyst: in both cases SPECT showed a congruent perfusion defect. Patient 3 suffered from Lennox-Gastaut syndrome and mental retardation; cerebral atrophy was seen on computed tomography and a SPECT pattern of multifocal cortical defects. Patient 4 presented with two inaugural consecutive tonic-clonic seizures. Both computed tomography and magnetic resonance imaging showed bilateral periventricular abnormalities, with the magnetic resonance imaging contrast suggesting demyelination. SPECT performed five days after the last seizure showed bilateral periventricular and left cortical hypoperfusion (figure (B)). Patient 5 who had tuberous sclerosis and mild periventricular calcifications shown on computed tomography, suffered from mental retardation and frequent tonic-clonic seizures. SPECT showed multiple cortical and subcortical areas of hypoperfusion.

(2) PATIENTS WITH NORMAL COMPUTED TOMOGRAPHY (N=9)

(a) With focus on electroencephalography

In patient 6 intractable complex partial seizures

Table 2 *Results of electroencephalography, computed tomography, and SPECT*

Patient No	*Electroencephalography*	*Computed tomography*	*Iodoamphetamine-SPECT*
1	Normal	Left sylvian porencephalic cyst	Left sylvian defect
2	Normal*	Right sylvian porencephalic cyst	Right sylvian defect
3	Bilateral slow spike-and-wave discharges	Cerebral atrophy	Multifocal cortical defects
4	Normal*	Bilateral periventricular hypodensities	Bilateral periventricular and left cortical hypoperfusion
5	Diffuse polyspike-and-wave	Periventricular calcifications	Multiple foci of hypoperfusion
6	Spikes at left temporal	Normal	Left temporal hypoperfusion
7	Normal	Normal	Normal
8	Normal	Normal	Normal
9	Normal*	Normal	Normal
10	Normal	Normal	Normal
11	Normal*	Normal	Extensive right hemispheric hypoperfusion
12	Normal*	Normal	Left temporal hypoperfusion
13	Diffuse polyspike-and-wave	Normal	Left parietal focus of hyperperfusion behind a hypoperfused area
14	Slow background	Normal	Bilateral foci of hypoperfusion

*Result at time of SPECT; previous electroencephalograms had shown diffuse polyspike-and-wave.

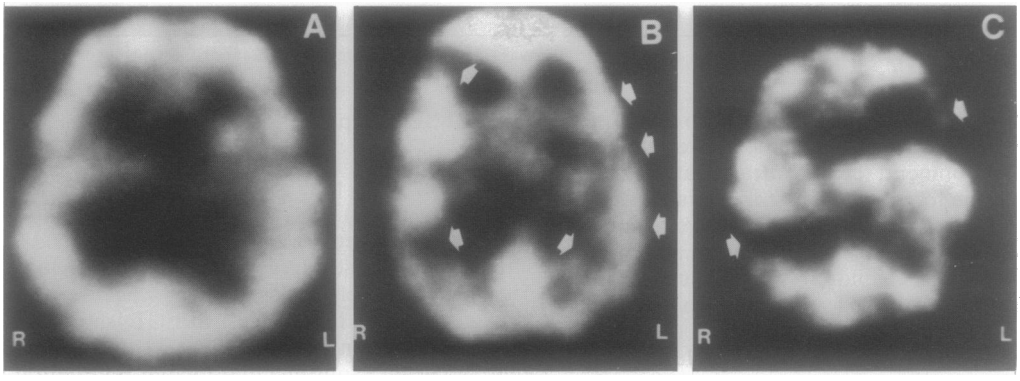

Figure *Transaxial SPECT images in three children with seizure disorders. Slice level is about 4 cm above the orbitomeatal line. A=normal tomography (patient 7); B=bilateral periventricular and left cortical hypoperfusion (patient 4); C=left frontotemporal and right parieto-occipital areas of hypoperfusion (patient 14).*

were attributed to a left temporal electroencephalographic focus. SPECT showed a focal abnormality consisting of a left temporal hypoperfusion.

(b) Without focus on electroencephalography
Patients 7 and 8 with rare Bravais-Jacksonian crisis, patient 9 with infrequent tonic-clonic seizures, and patient 10 who was studied four days after a first febrile tonic-clonic seizure, had normal electroencephalography and SPECT. Children 11 and 12 were seen, respectively, 12 hours and four days after a first tonic-clonic seizure when the electroencephalography was normal. SPECT showed an extensive right hemispheric hypoperfusion in patient 11 and a hypoperfusion limited to the left temporal lobe in patient 12. The electroencephalogram showed bilateral polyspike and wave in patient 13 who presented absences. Although the patient was asymptomatic at time of SPECT, there was an intense left parietal focus of increased uptake behind a hypoperfused area. Patient 14 had had severe neurological hypotonia since birth. Extensive examinations had failed to show any aetiology to that disorder, which is probably degenerative in nature. SPECT showed bilateral areas of hypoperfusion (figure (C)).

Discussion

In childhood epilepsy it is sometimes difficult to

confirm the existence of structural lesions, to assess the indication for an anticonvulsant treatment, and to predict the evolution of the disease in terms of frequency of seizures and mental development. This is due to the complexity of the underlying neurological processes, as shown by the numerous clinical forms, patterns on electroencephalography, and aetiological factors, and to the relative paucity of information provided by conventional procedures: deep epileptic foci are frequently missed by routine electroencephalography,[9] and computed tomography often fails to show small gliotic areas or cytoarchitectural changes.[4] Moreover anatomic abnormalities seen on computed tomography or magnetic resonance imaging do not always correlate well with clinical or electroencephalographic data.[10]

The early work of Plum *et al* has show that haemodynamic and metabolic changes were coupled during convulsions.[11] Using positron emission tomography, several authors have described a similar pattern of cerebral metabolism and cerebral blood flow in seizure disorders.[2 3] The study of the perfusion alone can therefore be considered as a good approach to metabolic pertubations in epilepsy.

Recently introduced techniques combining SPECT and flow tracers have been proposed as a particularly versatile, convenient, and low cost alternative to cerebral flow studies using positron emission tomography. The first available molecules were amines labelled with ^{123}I—iodoamphetamine and hydroxy iodo propanediamine—and have been extensively used in a wide variety of disorders of the central nervous system. They are now superseded by ^{99m}Tc hexamethyl propylene amine oxime (HMPAO), which is superior for several reasons, in particular because of a lower cost and a lower absorbed radiation dose, allowing the administration of higher activities and leading to a better image quality. When we started this study, however, it was not commercially available in Belgium. The brain distribution of ^{123}I iodoamphetamine is in first approximation flow dependent, but little is known about the metabolism of this tracer during seizures, and other factors might interfere.[5 12] Data obtained using ^{123}I iodoamphetamine and SPECT in adult epilepsy, however, were consistent with findings from positron emission tomography.[5 6]

The use of SPECT in the study of children raises specific problems. Firstly, the effect of brain maturation on SPECT pattern is considerable. For obvious ethical reasons normal controls cannot be studied. Our experience, however, is in agreement with the evolution described in positron emission tomography and ^{18}F-2-fluoro-2-deoxy-D-glucose, where an adult like pattern is settled after 1 year of age (even though cerebral metabolism remains with much higher absolute levels of several years).[13] Secondly, because the patients have to be kept perfectly immobile sedation is often required, and one can argue about the use of medication in a functional neurological study. Nevertheless, it is unlikely that SPECT regional distribution could be significantly influenced by single and low doses of barbiturates.[14–16]

In the five patients with radiological lesions, SPECT showed congruent or more extensive abnormalities. On the other hand, five of the nine children with normal computed tomography had an abnormal SPECT study. Two patients with generalised seizures, diffuse polyspike-and-wave, and a normal computed tomogram had a focal or a regional SPECT hypoperfusion. This is in agreement with Podreka *et al* who have found, using SPECT and HMPAO, a high incidence (78%) of abnormally perfused regions in tonic-clonic seizures.[17] In patient 10 with absences and bilateral polyspike-and-wave, there was a hyperperfused focus. Interictal focal hyperperfusion has been described in patients suffering from complex partial seizures during spontaneous interictal bursts of focal electrical discharges and,[18 19] more recently, in a patient studied several hours after a tonic-clonic seizure in a state of psychomotor agitation, impaired consciousness, and with generalised paroxysms shown on electroencephalography.[17]

The ability of SPECT imaging to detect lesions not visualised by conventional procedures has potential diagnostic, therapeutic, and prognostic implications. The discovery of an interictal focus of hypoperfusion of hyperperfusion could help to assess the epileptogenic nature of ictal like phenomena. A focal abnormality in children with absences or tonic-clonic seizures could target the treatment towards focal epilepsy. In intractable seizures, surgical procedures could integrate the data from SPECT: limited resection or corpus callosotomy might be proposed in focal or diffuse hemispheric involvement. An extensive SPECT impairment is probably associated with a severe brain dysfunction and a poor clinical evolution in terms of intellectual performance and seizure frequency. Indeed, in our limited series the SPECT pattern was intimately related to the clinical status: school difficulties, mental retardation, frequent seizures, and neurological deficit were found in eight of 10 patients with abnormal SPECT, and conversely, all children with normal SPECT had less than two seizures per year and normal neurological and intellectual development.

References

[1] Engel J Jr. The use of positron emission tomographic scanning in epilepsy. *Ann Neurol* 1984;**15** Suppl:S108–91.

[2] Kuhl DE, Engel J Jr, Phelps ME, Selin C. Epileptic patterns of local cerebral metabolism and perfusion in humans determined by emission computed tomography of ^{18}FDG and ^{13}NH3. *Ann Neurol* 1980;**8**:348–60.

[3] Engel J Jr, Kuhn DE, Phelps ME. Patterns of ictal and interictal local cerebral metabolic rate studied in man with positron computed tomography. In: Akimoto H, Kazamatzuri H, Seino M, *et al*, eds. *Advances in epileptology*. XIII th Epilepsy International Symposium. New York: Raven Press, 1982:282–6.

[4] Gastaut H, Gastaut JL. Computerized tomography in epilepsy. *Epilepsia* 1976;**17**:325–6.

[5] Hill TC, Holman BL, Lovett R, *et al.* Initial experience with SPECT (single-photon computerized tomography) of the brain using N-isopropyl l- 123 p- iodoamphetamine: concise communication. *J Nucl Med* 1982;**23**:191–5.

[6] Magistretti PL, Uren RF, Parker JA, Royal HD, Front D, Kolodny GM. Monitoring of regional cerebral blood flow by single photon emission tomography of l_{123}-n-isopropyl iodoamphetamine in epileptics. *Ann Radiol* 1983;**26**:68–71.

[7] Perlman JM, Herscovitch P, Kreusser KL, Raichie ME, Volpe JJ. Positron emission tomography in the newborn: effect of seizure on regional cerebral blood flow in an asphyxiated infant. *Neurology* 1985;**35**:244–7.

[8] Chugani HT, Mazziotta JC, Engel J Jr, Phelps ME. The Lennox-Gastaut syndrome: metabolic subtypes determined by 2-deoxy-2- ^{18}F-fluoro-D-glucose positron emission tomography. *Ann Neurol* 1987;**21**:4–13.

[9] Spencer SS, Spencer DD, Williamson PD, Mattson RH. The localizing value of depth electroencephalography in 32 patients with refractory epilepsy. *Ann Neurol* 1982;**12**:248–53.

[10] Theodore WH, Holmes MD, Dorwart RH, *et al.* Complex partial seizures: cerebral structure and cerebral function. *Epilepsia* 1986;**27**:576–82.

[11] Plum F, Posner JB, Troy B. Cerebral metabolic and circulatory responses to induced convulsions in animals. *Arch Neurol* 1968;**18**:1–13.

[12] Lucignani GR, Nehlig A, Blasberg R, *et al.* Metabolic and kinetic considerations in the use of (123) HIPDM for quantitative measurement of regional cerebral blood flow. *J Cereb Blood Flow Metab* 1985;**5**:86–96.

[13] Chugani HT, Phelps ME, Mazziotta JL. Positron emission tomography study of human brain functional development. *Ann Neurol* 1987;**22**:487–97.

[14] Wechsler RL, Dripps RD, Kety SS. Blood flow and oxygen consumption of the human brain during anesthesia produced by thiopental. *Anesthesiology* 1951;**12**:308–14.

[15] Smith AL, Wollman H. Cerebral blood flow and metabolism: effects of anesthetic drugs and techniques. *Anesthesiology* 1972;**36**:378–400.

[16] Theodore WH, DiChiro G, Margolin R, Fishbein D, Porter RJ, Brooks RA. Barbiturates reduce human cerebral glucose metabolism. *Neurology* 1986;**36**:60–4.

[17] Podreka I, Suers E, Goldenberg G, *et al.* Initial experience with technetium-99m HM-PAO brain SPECT. *J Nucl Med* 1987;**28**:1657–66.

[18] Bonte FJ, Stokely EM, Devous MD, Homan RW. Single photon tomographic study of regional cerebral blood flow in epilepsy: a preliminary report. *Arch Neurol* 1983;**40**:267–70.

[19] Lee BI, Markand ON, Siddiqui AR, *et al.* Single photon emission computed tomography (SPECT) brain imaging using N,N,N′-trimethyl-N′-(2 hydroxy-3-methyl-5-^{123}I-iodobenzyl)- 1, 3-propanediamine 2 HCL (HIPDM): intractable complex partial seizures. *Neurology* 1986;**36**:1471–7.

Correspondence to Dr R Denays, Department of Neurology, St Peter's Hospital, rue Haute 322, 1000 Bruxelles, Belgium.

Accepted 14 June 1988