TC-99m-HMPAO SPECT in PARTIAL EPILEPSY; Interictal Study in Thirty-Three Patients

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SUMMARY:

Tc-99m HMPAO SPECT brain imaging was performed interictally in thirty three patients with partial seizures. Identification of areas of low perfusion was by visual inspection in all patients and additionally in 16 patients quantitative values were obtained. SPECT results were compared with the EEG and CT. In 27 patients (82%), SPECT demonstrated decreased regional cerebral perfusion. Localised pathology in one hemisphere was shown in 21 patients with SPECT (63.6%), in 14 with EEG (42%) and in 9 with CT (27.2%). The areas that showed decreased perfusion were mostly correlated with EEG and/or CT findings. Tc-99m-SPECT can be useful in lateralisation of the epileptic area, especially in candidates for surgery.

KEY WORDS:

Partial epileps, SPECT, regional cerebral blood flow, Tc-99m-HMPA.

INTRODUCTION

In the last 10 years, parametric images of physiological brain processes such blood flow and metabolism can be obtained by the introduction of positron emission tomography (PET) and single photon emission computed tomography (SPECT) (11,28).

For 50 years, it has been known that cerebral blood flow increases during epileptic seizures in man (17,19,36,37). Also PET and SPECT ictal studies in epileptics have shown increased regional cerebral metabolic rate (rCMR) and regional cerebral blood flow (rCBF) in the epileptic focus (32,43,44,46). In the interictal studies, more conflicting results were obtained, most studies demonstrating regional perfusion decreases (6-8,12,19,27,30,31,43,48,49) but some showing increases (22,23,41).

When surgical intervention is considered for patients with refractory complex partial seizures, studies for lateralisation and localisation of epileptic tissue are necessary. PET and SPECT studies showed that these techniques could help to determine the epileptic area. Since PET scanning is complex, very expensive and likely to remain restricted to a few major centres, interest has grown in the potential of SPECT for the study of brain function in epilepsy.

New radiopharmaceuticals such as Technetium-99m hexamethylpropyleneamine oxime (Tc-'m-HMPAO) cross the blood brain barrier and distribute in the brain in proportion to regional blood flow (1,33,42). In most studies, rCBF and brain metabolism are closely linked (5,18,34,39). With Tc-99m-HMPAO SPECT brain images reflect rCBF and regional brain metabolism.

We report experiences with Tc-99m-HMPAO SPECT in thirty-three patients with partial epilepsy. These interictal SPECT results were compared with electroencephalography (EEG) and computerized tomography scan (CT) for evaluation for the value of determining of epileptic focus.

MATERIAL and METHOD

Patient population:

Thirty-three patients (19 female) with partial epilepsy meeting the selection criteria of the International League Against Epilepsy (ILAE) (9,10) underwent interictal Tc-99m-HMPAO-SPECT. The patients had a mean age of 315 years (range 18-60) and the duration of illness was 158 years (range 1 month-45 years). The probable cause was head trauma in 13 patients (cases 5,6,7,8,14,15,18,19,21,23,25,27,30), febrile convulsions in 4 patients (cases 6,17,24,33), and meningitis in one (case 13). Other chinical features of the patients are shown im Table 1).

Table 1 : Clinical, EEG, CT and SPECT findings of thirty three patients with partial epilepsy.

Case No	Sex	Age	Duration of illness (year)	Type of seizure	Frequency of seizure	Anticonvul-sant	EEG	CT	SPECT
1	F	23	16	SP*	very rare	DPH, Clon.	L PCT focus	Normal	L FP I ,R P I
2	M	20	5	CPE*	frequent	CBZ, Clon.	Bil. T. Par. act.	Normal	R T I
3	F	27	24	CPE	frexuent	CBZ	Bil. T. E. act.	Normal	R FT, L T I
4	M	39	18	CPE	frequent	DPH	Bil. T. foci	Min. Atrofi	irregular uptake
5	M	46	45	CPE*	frequent	CBZ, Prim.	L mid T. focus	Normal	Normal
6	M	24	17	CPE*	very frequent	CBZ, Prim.	Bil. T.E.act.	Normal	L.T. I
7	M	53	13	CPE*	rare	DPH, CBZ, Clon.	Bil. T. focus	Min. Atrofi	L T. I
8	M	28	3mo.	CPE*	rare	DPH	Normal	L PO lesion (Tm.?)	L TPO I
9	F	23	13	CPE	frequent	CBZ, Prim.	L CT. focus	Normal	L TO I
10	F	25	18	SP*	rare	DPH	Normal	Normal	L F. I
11	M	29	17	CPE	frequent	CBZ,BP,Prim.	Bil. F.T.E. act.	Normal	Bil. F. I
12	F	31	10	CPE	rare	CBZ	L T. Par. act.	Normal	L FP I
13	M	19	8	CPE	frequent	CBZ,Sod. Val.	R T., L FCT. focus	Normal	Normal
14	M	42	2	CPE	frequent	CBZ	Bil. FT. Par. act.	Bil. hipodenceles.	Irregular uptake
15	M	21	16	CPE*	rare	CBZ,DPH, Clon.	R FCT. focus	R TO infarct	R TO I
16	M	37	17	SP*	rare	DPH	Bil. FTP. par. act.	Normal	L TO I
17	M	18	10	CPE	frequent	CBZ,Prim.	L FT focus	L cystic les.	L T I
18	M	30	23	SP*	very rare	PB,DPH	L F. focus	L F. porencs. cyst	L F I
19	M	60	10	CPE*	very rare	—	Bil. T. par. act.	L T. atrophy	L PT I
20	F	35	1mo.	CPE*	frequent	DPH,PB	Normal	R FP hipodence les.	R TPO I
21	M	36	13	SP*	very frequent	DPH	R CPT focus	Normal	R TPO I
22	F	29	13	CPE	frequent	CBZ	Bil. FCT.E. act.	Normal	L T I
23	M	43	31	CPE*	very frequent	DPH,CBZ	Bil. CT. par. act.	L F.cronic inf.	L FT I
24	F	30	10	CPE	frequent	CBZ	Bil. T. E. act.	Normal	L T. I
25	F	18	17	CPS*	very frequent	CBZ,PB	Bil. FT. par. act.	Normal	L FPT I
26	F	27	25	CPE	very frequent	CBZ	Normal	Normal	L FT I
27	F	31	27	CPE*	frequent	CBZ,PB	L T. focus	L T. atrophy	L TP I
28	F	32	12	CPE*	very rare	CBZ	Normal	Normal	Normal
29	M	47	12	CPE*	very rare	CBZ,DPH	Normal	Normal	L PTO I
30	M	32	19	CPE*	frequent	DPH,CBZ	R.T.focus	Normal	R T I
31	M	40	35	SP*	very rare	DPH	Normal	Normal	Normal
32	F	23	12	SP*	frequent	DPH	generalized slow act.	R F. AVM	Normal
33	M	23	16	CPE*	very frequent	DPH,CBZ,Na.Val.	R mid T. focus	Normal	Normal

Abbreviations :

CBZ :Carbamazepine
DPH : Diphenylhydantoin,
Na Val : Sodium Valproat
PB : Phenobarbital
Clon : Clonazepam
Prim : Primidone
T : Temporal
F : Frontal
C : Central
P : Parietal
o : Occipital
Bil : Bilateral
E : Epileptiform
Act : Activity
Par : Paroxysmal
SP : Simple partial
CPE : Complex partial epilepsy
* : Secondary generalized seizures
Very rare : maximum 1 seizure in a year
Rare : 2-10 seizures in a year
Frequent : 1-5 seizures in a month
Very frequent: seizures approximately every day

The control group consisted of 5 healthy persons who had a mean age of 38 (range 3-51). Fifteen patients in the "SPECT in schizophrnia" study (26) were chosen as a second control group.

METHOD:

An 8-channel Grass model 8 electroencephalograph with scalp electrodes was used on all patients. 182 EEGs of 33 patients were reviewed for determination of the epileptic focus. The interval between the EEG and SPECT was maximum 5 months. CT scans with and without intravenous contrast material were done on all patients.

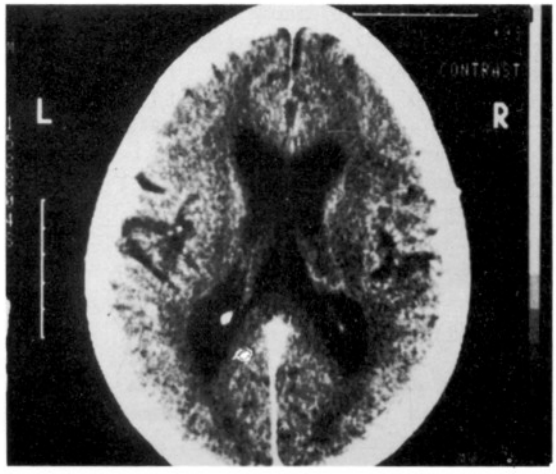

Fig 1: A) CT of patients 19 showing left temporal atrophy.

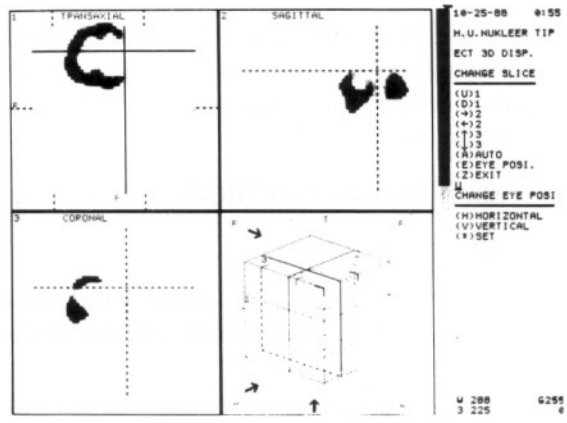

Fig 1 : B) Decreased rCBF in the left temporoperietal region was shown by brain SPECT of the same patient.

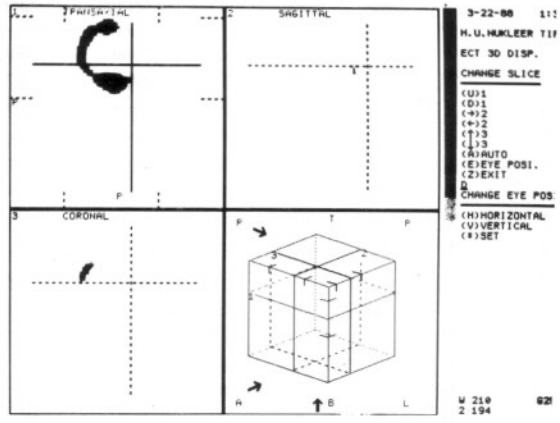

Fig 2: Brain SPECT of patients 25: When CT was normal brain SPECT showed decreased rCBF in the left frontotem poroparietal region.

SPECT : The patients were placed in a quiet room. HMPAO was prepared according to the manufacturer's recommendations by adding 20-30 mCi 99 m pertechnetate. The tracer was given intravenously (i.v) in the dosage of 15-20 mCi. Using a single head rotating gamma camera data acquisition started 10 min. after the i.v. injection. A parellel all purpose collimator of low resolution was used. Data was obtained in 60 projections through 360° each projection was stored as a 64x64 matrix with a pixel size of 5.6 mm. The acquisition time was set at 30 sec/projection. The date was preprocessed using a 5-point smoothing filter prior to reconstruction. Attenuation correction was not performed. Transverse, sagittal

and coronal images were generated in a thickness of 11.2 mm.

Areas showing decreased perfusion were interpreted visually. Additionally, the asymmetry index (AI) was calculated using mean counts/pixel in the ROI of the defected area and contralateral areas for 16 patients using the method "Region of Interest" (ROI) (16).

AI was also calculated for control groups.

$$\text{ASYMMETRY INDEX: } 100X \frac{\text{affected area - contralateral area}}{\text{contralateral area}}$$

For the statistical analysis of data, the MacNemar test was used. Difference of mean asymmetry index between patient and control group was defined using unpaired Student's t-test.

RESULTS

The results are shown in Table 1.

The lateralisation with clinical features of seizures was made on anly 7 patients (21.2%) (cases 1,10,16,18,21,23,32).

In 14 cases (cases 1,4,5,7,9,12,13,15,17,18,21, 27,30,33) the epileptic focus could be identified by EEG with scalp electrodes (42.4%). The EEG showed bilateral foci in three cases (cases 4,7,13) and was normal in 6. In the rest of the patients, the EEG showed bilateral nonspecific paroxysmal discharges (Table 1).

CT was normal in 21 patients (63.7%). CT scans of 12 patients were pathological (36.3%) and in 9 of these the pathology localised in only one hemisphere (27.2%).

When AI showed values of 10 or higher it was considered pathological (38). The mean value of AIs for 5 healthy subjects was 4+0.7; for schizophrenic cases, 2.06+1.7.

Twenty-seven patients had a region of focal hypoperfusion (82%). A focal or lateralized hypoperfusion in only one hemisphere was seen on the SPECT of 21 patients (63.6%). In 4 cases SPECT showed hypoperfusion homologous regions of the hemispheres. Irregular uptake was shown in 2 patients. SPECT was normal in 6.

Postictal SPECT was obtained in cases 11 and 32 (cases 11 also had hypoperfusion in the same area shown by interictal SPECT). Case 32 had only postictal SPECT and it was normal. The comparison of SPECT with EEG and CT is summarized in Tables 2 and 3. For the detection of pathology, SPECT is more valuable than CT (X^2 = 11.52941, sensitivity: 40.7%, specificity 83.3%, positive predictive value: 91.7%, negative predictive value: 23.8%). SPECT and EEG had no significant difference in detection of pathology (X^2 = 0.12) (sensitivity: 85.2%, specificity: 33.3%, positive predictive value: 85.2%, negative predicting value: 33.3%). In lateralistaion, differences between EEG and SPECT were significant (X^2 = 4.9) (sensitivity: 83.3%, specificity: 47.1%, positive predicting value: 35.7%, negative predicting value: 88.9%).

Table 2 : Comparison of SPECT with EEG

		SPECT		
		Bilateral	**Unilateral**	**Normal**
EEG	Bilateral	5 (15.5%)	9 (27.2%)	2 (6%)
	Unilateral	1 (3%)	8 (24.2%)	2(6%)
	Normal	–	4 (12.1%)	2 (6%)

Table 3 : Comparison of SPECT with CT

		SPECT		
		Bilateral	**Unilateral**	**Normal**
CI	Bilateral	2 (6%)	1 (3%)	–
	Unilateral	–	8 (24.2%)	1 (3%)
	Normal	4 (12.2%)	12 (36.6%)	5 (15.5%)

Table 4 : Interictal studies with SPECT

Number of cases		Tracer	rCBF
1		IMP	I Kuhl (1982)
18	IV	Xe-133	12/18 I Bonte (1983)
8		IMP	7/8 I Uren (1983)
3		IMP	2/3 I Bruine (1986)
4		HIPDM	3/4 I Lee (1986)
15	Tc-99 m	HMPAO	12/15 I Biersack (1986)
10	Tc-99 m	HMPAO	5/10 I Stefan (1987)
45	Tc-99 m	HMPAO	29/45 I Rowe (1986)
6	Tc-99 m	HMPAO	6/6 I Ell (1989)

DISCUSSION

Interictal PET and SPECT studies usually show decreased regional hypometabolism, rCBF (6-8,12,27,31,40,43,46,48): but Hougaard at al, and Sakai et al, reported increased rCBF in epileptics with Xe-133 in the interictal period (23,41). In recent studies with patients who had partial seizures, it was reported that epileptics had increased rCBF at 5 percent (22). None of our patients had increased rCP. Other interictal SPECT studies are summarized in Table 4.

What is the reason for the decreased rCBF?

Pathological studies of the surgical specimens showed hamartoma focal gliosis or hipocampal sclerosis correlating with PET and/or SPECT findings in epileptics (14,31,44). Autopsies or surgical specimens from epileptics also showed arteriovenous malformations, astrocytoma or glioma (15).

Pathological dendrites, microvasculatory changes (thickness of the basal laminae, decreased endothelial mitochondria) and synaptic abnormalities were reported in the ultrastructural pathological study of the epileptic hippocampus (4,25).

Magnetic resonance imaging (MRI) can show glioma or mesial temporal sclerosis in epileptics when CT scans are normal (20,24,29,35,43,46).

Decreased rCBF is probably due to neuronal loss and/or microvasculatary changes.

SPECT and EEG

EEG with scalp electrodes helped to determine the epileptic focus in 14 patients (42.4%). Although we could not perform advanced electropysological studies such as long term monitorisation or EEG with deep electrodes because these techniques were no available and our patients are not candidates for surgery at present. On the other hand, we were lucky to review an average of 5 EEGs for each patient. We found that decreased rCBF shown by SPECT was larger than the epileptic focus shown by EEG. In the experimental animal model, when the convulsant drug was applied topically to the brain, it was shown by the contact auto radiography that the metabolism of the larger area was changed (7).

Case 1 had right parietal hypoperfusion in addition to the left frontoparietal hypoperfusion correlating with the EEG and clinical findings. Other interictal SPECT and PET studies also showed hypometabolism of the distant areas (11,30,32,45). The exact mechanism is not known but. Theodore et al. claimed thet some anticonvulsant drug might be responsible (45).

SPECT and CT

It was reported that CT could demonstrate pathology in 30-50 percent of patients with partial epilepsy (34,36). In our study. CT showed pathology in 12 patients (36.%): localized in one hemisphere in 9(27%).

In all patients (except case 32). SPECT showed hypoperfusion on the same localization found pathological by CT, but covering a larger area. Other reports, like ours, found areas showing decreased perfusion larger than the lesion shown by CT (45-47). The cause may be different spatial resolutions between the SPECT and CT.

Case 32 had right frontal haematoma due to a small arteriovenous malformation. The postictal SPECT was normal. Ictal increasing might begin to decrease and the relative decreased perfusion seen as a normal perfusion could be obtained (3).

In our study. SPECT was found to be superior to CT scan for detection of pathology and to EEG with scalp electrodes for lateralization of epileptic focus (SPECT 63.6%, EEG 42.4%, CT 27.2%). It is difficult to compare our findings with the results of other reports because of the different tracers, number of patients and EEG technique. Stefan et al. reported on ten patients with partial epilepsy to whom were applied interictal PET, CT, MRI, Tc-99 m-HMPAO SPECT, EEG (43). Their study showed lateralized pathology in 10 patients with PET, 8 with MRI, 7 with EEG, 5 with SPECT, 3 with CT. Superiority of EEG to SPECT was probably due to EEG with long term monitorisation and sphenoidal electrodes. Other reports agreed that SPECT and PET are superior to CT (15,21,30,43;46;47;49).

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