Regional cerebral blood flow of patients with focal epilepsy studied using xenon enhanced CT brain scanning

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SUMMARY Stable xenon-enhanced X-ray computed tomography (XeCT) was used to measure the regional cerebral blood flow (rCBF) of 12 patients with drug resistant partial epilepsy and a marked unilateral focus on electroencephalography (EEG). Interictal mean rCBF of fixed regions of interest (ROIs) was reduced by 25% in the cortex of the epileptogenic cerebral lobe compared with the same regions on the contralateral side ($p < 0.02$). Six control scans showed a mean side to side cortical difference in rCBF of 14%, whereas the epileptogenic focus was associated with a reduction in the cortical rCBF of greater than 30% in six out of the 12 patients. In an additional patient with partial epilepsy XeCT demonstrated significant focal hypoperfusion when interictal EEGs and conventional CT scans showed no abnormalities.

Stable xenon-enhanced X-ray computed tomography (XeCT) has previously been used to measure regional cerebral blood flow (rCBF) in normal subjects,¹ and patients with cerebrovascular disease.^{2,3} In a group of 19 resting normal subjects no significant differences between the rCBF of left and right cerebral structures were found.¹ To date there have been no reported measurements using XeCT of rCBF in patients with focal epilepsy.

Regions of hypometabolism have been demonstrated interictally in approximately 50-70% of patients with focal epilepsy studied with positron emission tomography (PET).⁴⁻⁶ Such regions correspond most frequently to foci of mesial temporal sclerosis, although the areas of hypometabolism are generally found to be more extensive than the histological lesions. This is likely to be caused by the inactivation of associated structures.⁷

The presence of mesial temporal sclerosis is of clinical significance because these epileptic patients have a much better prognosis following surgery than patients without histological abnormalities.⁸ Consequently the detection of focal hypometabolism in patients with partial epilepsy may be of prognostic value. Metabolic studies using PET have demon-

strated focal abnormalities in patients with partial epilepsy that were not apparent from EEGs.⁹ PET, however, is not yet widely available and while single photon emission computed tomography (SPECT) may also be able to demonstrate changes in rCBF in patients with focal epilepsy, absolute flow values cannot readily be computed using this technique.¹⁰

At present the preoperative localisation of epileptic foci is usually based on a combination of clinical features, routine and specialised EEGs, and radiology. Unfortunately good quality ictal EEG recordings cannot always be obtained. In this study we demonstrate the use of the potentially widely available XeCT technique as an adjunct to EEG in localising interictal regions of hypoperfusion in patients with focal epilepsy.

Subjects

The details of the 12 patients with focal epilepsy are listed in table 1. The six control XeCT scans were obtained from five patients with generalised seizures who were not suitable for surgical treatment because of both the clinical and EEG findings. Four controls had generalised 3 per second spike and wave activity on ictal EEGs. The fifth control had bilateral abnormalities on psychometry, generalised spikes on his interictal EEG, and no focal discharges during sphenoidal ictal recordings. An additional patient was studied who had stereotyped partial seizures. Her interictal EEGs showed no abnormalities and ictal recordings could not be obtained because of relatively long periods between seizures. Three

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Table 1 Characteristics of patients with focal EEG abnormalities

Patient number	Age (yr)	Sex	Febrile seizure	Features of seizure	EEG focus	Site of CT lesion
1	19	F	Yes	Left sided jerking Automatism	Right anterior temporal*	None
2	34	F	No	Blank stare Postictal dysphasia	Left anterior temporal*	None
3	30	F	Yes	Blank stare Automatism	Deep right temporal*	None
4	28	F	No	Right sided jerking Automatism	Deep left temporal*	Left temporal
5	31	M	No	Automatism Postictal dysphasia	Left anterior temporal*	None
6	18	M	Yes	Blank stare Automatism	Right anterior temporal	Dilated R temporal horn
7	34	M	No	Blank stare Postictal dysphasia	Left anterior temporal	None
8	23	F	Yes	Blank stare Automatism	Right anterior temporal*	None
9	21	F	No	Right sided jerking Postictal dysphasia	Widespread left temporal	None
10	48	M	No	Confused thinking for a few seconds Attacks cluster	Right frontal	Dilated posterior horns
11	18	M	No	Eyes turn to right	Left frontal*	Left frontal
12	30	M	Yes	Brief kicking both legs	Left frontal	Left frontal†

*Denotes an ictal EEG recording.

†Denotes MRI localisation.

further patient studies had to be excluded: one patient had an aura on commencing the test and the procedure was abandoned, and two patients moved during the procedure to such an extent that a reliable functional image could not be produced. All patients had had multiple EEGs, usually including sleep and prolonged telemetry. Sphenoidal electrodes and corticography were used when clinically indicated. Patient's seizure frequencies ranged from 1–100 per month. All subjects were clinically seizure free for at least 6 hours prior to the study.

Methods

This study had the approval of the Ethics Committee of The National Hospital for Nervous Diseases, and all patients gave their informed consent. rCBF was measured using XeCT scanning as described by Yonas *et al.*² Scans were performed at 80kV, 200mAS with an IGE 9800 CT/T scanner using the commercially available CBF programme. Patients 1–12 were scanned in the plane containing the EEG focus. The slice position and angulation for temporal scans was determined so as to pass along the axis of the temporal lobe, avoiding the dense petrous bone and minimising artefactual streaking due to beam hardening. Typically the slices were angled 10–15° caudal from the orbito-meatal line. In two patients a slice position 1 cm superior to the axis of the temporal lobe was used. In patient 2 this reduced bone streak artefact, and in Patient 4 this included the small area of low attenuation that had been shown on previous CT scans. Frontal scans were performed in the plane most appropriate to the focus, typically using reverse gantry tilt of 10°. Patient 5 had to be rescanned because his first study included little temporal lobe tissue.

Lateral and medial temporal regions of interest (ROI) of 7–10 cm² were defined symmetrically for the two hemispheres by one of us (TL) from the anatomical scan (see fig 1), with-

out knowledge of the clinical, EEG or rCBF findings. Lateral regions of interest were defined as follows: 1cm width strips were used starting 1cm posterior to the anterior border of the temporal lobe. The strips extended posteriorly as far as the level of the trigone. The lateral border of each strip was subsequently positioned 3mm medial to the lateral mar-

Fig 1 The left lateral and medial strips of Patient 6 on the anatomical scan.

Table 2 The rCBF (ml/min/100g brain tissue) measured by XeCT in planes that included the EEG focus

Patient number	Lateral strip		Medial strip	
	Unaffected side	Affected side	Unaffected side	Affected side
1	83	48	50	46
2	60	41	40	42
3	37	35	43	29
4	67	57	58	49
5	69	43	37	27
6	65	40	52	35
7	34	38	22	9
8	48	61	53	53
9	70	58	30	38
10	72	35	32	28
11	79	54	73	69
12	90	80	70	65
Mean	65†	49	47*	41

†p < 0.02; *p < 0.05, Bonferroni statistics.

gin of the functional image. These dimensions were chosen to include as much of the temporal cortex as possible while minimising the inclusion of bone streak artefacts. Medial ROIs were placed contiguous to the lateral ROIs. They extended to the lateral border of the cavernous sinus. Frontal ROIs were similarly constructed as appropriate to the anatomical scan.

Both medial and lateral ROIs contained a mixture of grey and white matter. Approximately 50% of the lateral strips constituted peripheral cortical grey matter while the medial strips were a mixture of grey matter, white matter, and may on some occasions have included ventricle. It is likely that the medial strips contained less grey matter than the lateral strips. Once defined anatomically the ROIs were applied to the functional image and a printout of rCBF obtained. The hemisphere containing the EEG focus was designated the affected side, and the other hemisphere was designated the unaffected side. The percentage side to side difference was defined as: (higher side-lower side)/higher side $\times$ 100%.⁵

Results

The rCBF results are shown in tables 2 and 3. An example of XeCT is shown in fig 3. The patient group had a mean 25% reduction in the rCBF of the lateral strips on the affected side. The control group showed a mean 14% (SD = 8%) side to side difference in rCBF between lateral strips. In six of the patients with partial epilepsy the rCBF of the lateral strip on the affected side was reduced by more than 30% (control mean + 2 SD) compared with the normal side (fig 2). The percentage reduction in the rCBF of the medial strips on the affected side was only 13% in the patients with partial epilepsy. The control group showed a mean side to side difference in rCBF of 16% (SD = 10%) for the medial strips.

Case report

Patient 18 was a 45 year old women with a 20 year history of attacks of altered consciousness. These usually started with

Table 3 Control rCBF values (ml/min/100g tissue)

Patient number	Plane	Lateral strip		Medial strip	
		Right	Left	Right	Left
13	Mid temporal	59	71	52	63
14	Mid temporal	34	26	14	20
15	Mid temporal	34	30	29	24
15	Inf. frontal	37	32	24	32
16	Mid temporal	57	69	60	61
17	Mid temporal	42	42	23	25
Mean		44	45	34	38

an aura of epigastric discomfort which spread up into the chest and neck, followed by a tingling sensation in the neck. A few seconds later she would turn her head to the left and then have a generalised convulsion. These attacks would last for about 5 minutes, and occurred approximately once a month in spite of anticonvulsant treatment. She had more frequent isolated epigastric auras that lasted for up to 3 minutes. There were no definite clinical, psychometric or CT lateralising features, and four interictal EEGs, including a sleep study, were within normal limits. XeCT scan in the midtemporal plane showed hypoperfusion of the right temporal lobe (fig 4) with right lateral and medial rCBF values of 40 ml/min/100g compared with left lateral and medial values of 63 and 53 ml/min/100g respectively.

Fig 2 The percentage side to side differences in rCBF of the lateral strips for patients and controls. Key: ● Affected side < unaffected side, ○ Affected side > unaffected side, ▲ Control subjects, --- mean + 2 SD of controls.

Fig 3 The XeCT of Patient 6.

Discussion

We have shown that XeCT can identify areas of hypoperfusion associated with epileptogenic foci. In six out of 12 patients with partial epilepsy the rCBF of affected cortex was reduced by more than 30% compared with the contralateral cortex. In a seventh patient with partial epilepsy, normal interictal EEGs, and normal temporal and frontal lobes on CT scanning, the XeCT technique identified a temporal focus of hypoperfusion, the rCBF being 37% lower on the affected side.

In agreement with previous workers^{2,3} we found that XeCT was tolerated reasonably well. During xenon inhalation five patients became lightheaded, and one felt as though she was looking down a yellow tunnel. These symptoms resolved immediately after xenon inhalation ceased. One patient had an absence seizure following XeCT. It was noted that she was hyperventilating and this had often precipitated previous attacks.

Gur *et al* found that the main disadvantages of XeCT were low signal to noise ratio and artefacts produced by patient movement,¹¹ and this was also our experience. The first would be improved by using higher concentrations of xenon but this could lead to anaesthesia. The second requires careful selection of patients who are highly motivated and compliant. Using the IGE CBF protocol our data suggest that a side to side difference of more than 30% in rCBF between lateral strips is clinically significant.

Functional imaging is unable to delineate the exact

seat of EEG foci because regional hypofunction extends to associated structures. The lateral ROIs in the affected hemispheres of our patients with partial epilepsy demonstrated hypoperfusion more effectively than the medial ROIs. We suggest two possible explanations for this finding. Firstly, if an epileptic focus exerts maximal depression of function on cortex then it would be reasonable to expect the rCBF of the lateral ROIs to be more depressed than that of medial ROIs because lateral ROIs contain more grey matter. Secondly, in control subjects medial ROIs show a greater scatter in percentage side to side rCBF differences than lateral strips. This increased scatter in medial ROIs is probably a consequence of increased tissue heterogeneity and could obscure hypofunction. In practice we suggest that attention is focused on lateral rather than medial ROIs when rCBF side to side differences are being measured as part of the pre-operative work up of patients with partial seizures.

Three patients have now been treated surgically. Patient 6, with a right temporal focus on his XeCT, has been seizure free for 5 months following a right temporal lobectomy. Histology showed mild neuronal loss, and no vascular abnormality. Patient 11, with a left frontal focus on XeCT, was found to have a small supero-lateral frontal glioma and corticography revealed widespread left frontal discharges. Patient 12, with a normal XeCT, was found to have a small area of gliosis in the left medial frontal region, and corticography showed discharges confined to this region. Both patients 11 and 12 have been seizure free for the first postoperative month.

Our study suggests that XeCT may be a useful adjunct in the assessment of patients with intractable

Fig 4 The XeCT of Patient 18.

partial epilepsy. We are performing further studies on patients with focal and generalised epilepsy, and will correlate XeCT with surgical findings and outcome.

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References

- 1 Tachibana H, Meyer JS, Okayasu H, Kandula P. Changing patterns of cerebral blood flow with age measured by xenon CT. *AJR* 1984;142:1027-34.
- 2 Yonas H, Wolfson SK, Gur D, *et al.* Clinical experience with the use of xenon-enhanced CT blood flow mapping in cerebral vascular disease. *Stroke* 1984;15:443-50.
- 3 Meyer JS, Hayman LA, Takahiro A, *et al.* Mapping local cerebral blood flow in humans during xenon inhalation. *Stroke* 1981;12:426-36.
- 4 Engel J, Kuhl DE, Phelps ME, Mazziotta JC. Interictal cerebral glucose metabolism in partial epilepsy and its relation to EEG changes. *Ann Neurol* 1982;12:510-7.
- 5 Theodore WH, Brooks R, Sato S, *et al.* The role of positron emission tomography in the evaluation of seizure disorders. *Ann Neurol* 1984;15S:S180-90.
- 6 Sperling MR, Wilson G, Engel J, Babb TL, Phelps M, Bradley W. Magnetic resonance imaging in intractible partial epilepsy: correlative studies. *Ann Neurol* 1986;20:50-62.
- 7 Engel J, Brown WJ, Kuhl DE, Phelps ME, Mazziotta JC, Crandall PH. Pathological findings underlying focal temporal hypometabolism in partial epilepsy. *Ann Neurol* 1982;12:518-28.
- 8 Falconer MA, Serafetinides EA. A follow up study of surgery in temporal lobe epilepsy. *J Neurol Neurosurg Psychiatry* 1963;26:154-65.
- 9 Engel J, Kuhl DE, Phelps ME, Crandall PH. Comparative localisation of epileptic foci in partial epilepsy by PCT and EEG. *Ann Neurol* 1982;12:529-37.
- 10 Lee BI, Markland ON, Siddiqui AR. Single photon emission computed tomography brain imaging using N,N,N'-1, 3-propanediamine 2HCl (HIPDM): Intractable complex partial seizures. *Neurology* 1986;36:1471-7.
- 11 Gur D, Wolfson SK, Yonas H, *et al.* Progress in cerebral vascular disease: local cerebral blood flow by xenon enhanced CT. *Stroke* 1982;13:750-8.

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