tion of [18F]-L-6-fluorodopa and its metabolites in blood plasma is essential for accurate positron emission tomography studies. *Life Sci* 1992;50:309–318.
17. Martin WRW, Palmer MR, Patlak CS, Calne DB. Nigrostriatal function in human studied with positron emission tomography. *Ann Neurol* 1989;26:535–542.
18. Patlak CS, Blasberg RG. Graphical evaluation of blood-to-brain transfer constants from multiple-time uptake data. Generalizations. *J Cereb Blood Flow Metab* 1985;5: 584–590.
19. Patlak CS, Blasberg RG, Fenstermacher JD. Graphical evaluation of blood-to-brain transfer constants from multiple-time uptake data. *J Cereb Blood Flow Metab* 1983;3:1–7.
20. Tedroff J, Aquilonius SM, Laihinen A, et al. Striatal kinetics of [11C]-(+)-nomifensine and 6-[18F]fluoro-L-dopa in Parkinson's disease measured with positron emission tomography. *Acta Neurol Scand* 1990;81:24–30.
21. Brooks DJ, Salmon E, Mathias CJ. The relationship between locomotor disability, autonomic dysfunction and the integrity of the striatal dopaminergic system in patients with multiple system atrophy, pure autonomic failure and Parkinson's disease studied with PET. *Brain* 1990;113:1539–1552.
22. Hoshi H, Kuwabara H, Léger G, Cumming P, Guttman M, Gjedde A. 6-[18F]fluoro-L-DOPA metabolism in living human brain: a comparison of six analytical methods. *J Cereb Blood Flow Metab* 1993;13:57–69.
23. Leenders KL, Palmer AJ, Quinn N, et al. Brain dopamine metabolism in patients with Parkinson's disease measured with positron emission tomography. *J Neurol Neurosurg Psychiatr* 1986;49:853–860.
24. Scheffé H. *The analysis of variance*. New York: Wiley; 1959:221–260.
25. Chan GL, Morrison KS, Holden JE, Ruth TJ. Plasma L-[18F]6-fluorodopa input function: a simplified method. *J Cereb Blood Flow Metab* 1992;12:881–884.
26. Boyes BE, Cumming P, Martin WRW, McGeer EG. Determination of plasma 18F-fluorodopa during positron emission tomography: elimination and metabolism in carbidopa treated subjects. *Life Sci* 1986;39:2243–2252.
27. Kish SJ, Shannak K, Hornykiewicz O. Uneven pattern of dopamine loss in the striatum of patients with idiopathic Parkinson's disease. *N Engl J Med* 1988;318:876–880.
28. Brooks DJ, Ibanez V, Sawle GV, et al. Differing patterns of striatal [18F]-dopa uptake in Parkinson's disease, multiple system atrophy, and progressive supranuclear palsy. *Ann Neurol* 1990;28:547–555.
29. Carson RE. Precision and accuracy considerations of physiological quantitation in PET. *J Cereb Blood Flow Metab* 1991;11:A45–A50.
30. Takikawa S, Dhawan V, Chaly T, et al. Input functions for 6-[fluorine-18]fluorodopa quantitation in parkinsonism: comparative studies and clinical correlations. *J Nucl Med* 1994;35:955–963.
31. Sawle GV, Playford ED, Burn DJ, Cunningham VJ, Brooks DJ. Separating Parkinson's disease from normality. Discriminant function analysis of fluorodopa F-18 positron emission tomography data. *Arch Neurol* 1994;51:237–243.
32. Powers WJ, Berg L, Perlmutter JS, Raichle ME. Technology assessment revisited: does positron emission tomography have proven clinical efficacy? *Neurology* 1991; 41:1339–1340.
33. Therapeutics and Technology Assessment Subcommittee. Assessment: positron emission tomography. *Neurology* 1991;41:163–167.
34. Burn DJ, Sawle GV, Brooks DJ. Differential diagnosis of Parkinson's disease, multiple system atrophy and Steele-Richardson-Olszewski syndrome: discriminant analysis of striatal 18F-dopa PET data. *J Neurol Neurosurg Psychiatry* 1994;57:278–284.
35. Vingerhoets FJG, Snow BJ, Tetrud JW, Langston JW, Schulzer M, Calne DB. Positron tomography evidence for progression of human MPTP-induced dopaminergic lesions. *Ann Neurol* 1994;36:765–770.

Increased Contralateral Cerebellar Uptake of Technetium-99m-HMPAO on Ictal Brain SPECT

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Crossed cerebellar diaschisis (CCD) is a well-known brain SPECT finding in stroke patients. Two reports, however, have described supratentorial and contralateral cerebellar hyperperfusion (crossed cerebellar hyperperfusion) on ictal brain SPECT in epileptic patients. The purpose of this study was to assess the usefulness of crossed cerebellar hyperperfusion (CCH) for the detection of epileptic foci on ictal scan. **Methods:** Twelve patients with complex partial seizures having characteristic clinical, electroencephalographic (EEG) and brain SPECT findings were included. Fifteen to 20 mCi ^{99m}Tc-HMPAO were injected intravenously during the seizure period or the aura for the ictal SPECT study. The SPECT findings were visually assessed to determine whether the finding of CCH was valuable in the localization of ictal foci. **Results:** Epileptic foci were found in the right temporal (n = 6), left temporal (n = 4), right occipital (n = 1) and left frontal (n = 1) areas. CCH was observed in 8 (75%) of the 12 patients. In two patients, contralateral cerebellar uptake was more obvious than that in the epileptic foci. In the interictal scans, cerebellar activity, which was increased in ictal period, was equalized in seven of eight patients, while perfusion was diminished in the remaining patient. **Conclusion:** CCH is a frequent finding of ictal brain SPECT and may aid in the lateralization of epileptic foci.

Key Words: epilepsy; SPECT; crossed cerebellar hyperperfusion
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Seizure disorder is classified into partial and generalized forms. Partial seizures begin in a part of one hemisphere. Generalized seizures, on the other hand, are those in which the first clinical changes indicate initial involvement of both hemispheres (*1*). Partial seizures are classified as simple when consciousness is not impaired and as complex when consciousness is impaired (*1*). Medically intractable complex partial seizure is a good indication for surgical treatment; therefore, identification of epileptic focus in complex partial seizures is essential for surgical treatment (*2*). EEG, electrocorticography (ECoG) and MRI have all been used for the lateralization of epileptic foci (*2,3*). SPECT and PET have also proved to be important diagnostic tools (*4–6*). Recently, cerebral perfusion SPECT studies are widely available in conjunction with EEG data, which show high corresponding diagnostic rates in the localization of epileptic foci (*6–9*). In general, hyperperfusion or hypermetabolism is detected ictally and hypoperfusion or hypometabolism is detected interictally in ictal focus (*6,7,9*).

Crossed cerebellar diaschisis (CCD), the phenomenon of reduction of blood flow in the contralateral cerbellum due to supratentorial lesion in stroke patients, was first described by Baron et al. in 1980 using PET (*10*). Much the same as CCD in the mechanism of cerebral and cerebellar metabolic connection, supratentorial and contralateral cerebellar hyperperfusion (crossed cerebellar hyperperfusion, CCH) was sporadically reported in patients with seizures during the ictal phase (*11,12*).

The aim of our study was to evaluate the characteristic findings of CCH and to assess the usefulness of the finding for the localization of epileptic foci on the ictal scan.

MATERIALS AND METHODS

Twelve patients (9 men, 3 women; aged: 4–52 yr; mean 20 yr) with medically intractable complex partial seizures having congruent clinical, EEG and brain SPECT findings were studied.

Seven patients underwent surgical therapy: temporal lobectomy in five and occipital cortisectomy and callosotomy (anterior 2/3) in

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TABLE 1
Clinical Data and SPECT Findings

Patient no.	Sex	Age (yr)	EEG	Morphological lesions (CT, MRI)	Ictal SPECT			Interictal SPECT		Surgery and pathology
					Epileptogenic lesion		Contralat. cerebellum	Ictal focus	Contralat. cerebellum	
1	M	31	Rt. F-T	CT (N)	Rt. T	Increased	N	Decreased	N	Not done
2	M	10	Rt. F-T	CT (N)	Rt. T	Increased	Increased	Equalized	Equalized	Not done
3	M	27	Rt. T	MRI (Rt. MTS)	Rt. T	Increased	N	Equalized	Decreased	Rt. temporal lobectomy; gliosis
4	M	35	Rt. T	MRI (N), CT (N)	Rt. T	Increased	Increased	Equalized	Equalized	Rt. temporal lobectomy; normal
5	M	30	Lt. T	MRI (Lt. MTS)	Lt. T	Increased	Increased	Decrease	Equalized	Lt. temporal lobectomy; gliosis
6	M	16	Rt. T	CT (N)	Rt. T	Increased	Increased	Equalized	Equalized	Callosotomy (Anterior 2/3)
7	M	27	Lt. F-T	CT (N)	Lt. T	Increased	N	Equalized	N	Not done
8	M	4	Lt. F	MRI (N)	Lt. F	Increased	Increased	Decreased	Decreased	Not done
9	F	17	Rt. Occi	CT (N)	Rt. Occi	Increased	Increased	Equalized	Equalized	Rt. occipital cortisectomy
10	F	52	Lt. T	CT (N)	Lt. T	Increased	N	Not done		Not done
11	F	30	Rt. T	MRI (N)	Rt. T	Increased	Increased	Decreased	Equalized	Rt. temporal lobectomy; gliosis
12	M	34	Lt. T	MRI (N)	Lt. T	Increased	Increased	Decreased	Equalized	Lt. temporal lobectomy; gliosis

F-T = frontotemporal; F = frontal; T = temporal; Occi = occipital; MTS = mesial temporal sclerosis; N = no abnormality.

one each. MRI was performed in six patients. Mesial temporal sclerosis was found in two patients but was normal in four. The remaining six patients underwent brain CT which did not show any structural abnormality.

All patients underwent surface scalp EEG and electrocorticography was obtained in two. For the ictal scans, anticonvulsants were discontinued and patients were monitored by continuous video-EEG monitoring. HMPAO and [^{99m}Tc]pertechnetate were prepared at the bedside. When seizure or aura developed, HMPAO was reconstituted with 15–20 mCi (0.25 mCi/kg) [^{99m}Tc]pertechnetate for 30 sec and then injected intravenously. Patients were transported to the nuclear medicine unit for scanning within 1 hr postinjection.

The scanning procedure was performed by using a single or a dual-head gamma camera equipped with high-resolution, low-energy, pararell-hole collimators. Sixty-four projections with an aquisition time of 40 sec/view were acquired in 64 × 64 martices with a 5.6° angular increment. Transaxial images were obtained by the filtered backprojection method using a Butterworth filter (Nyquist frequency 0.35 cycle/cm at an order of 5) and coronal and sagittal images were reconstructed. The slice thickness was 5.8 mm.

Follow-up interictal scans were obtained in 11 patients for at least three days after the ictal scan. The SPECT findings were visually interpreted by two experienced nuclear medicine specialists who were blinded to the EEG findings.

RESULTS

Epileptic foci were found as an area of hot activity in the right temporal (n = 6), left temporal (n = 4), right occipital (n = 1), and left frontal (n = 1) areas (Table 1). CCH was observed in 8 (75%) of the 12 patients on the ictal scans: right temporal in four, left temporal in two, right occipital in one and left frontal in one patient (Fig. 1, Table 2).

In the remaining four patients, increased uptake in the cerebellum was not observed (Table 1). In two of the eight patients with CCH, the cerebellar uptake was more obviously increased than that in the epileptic foci (Fig. 2).

In 5 of 11 patients, interictal SPECT revealed diminished uptake in epileptic foci. Equal cerebellar activity was seen in seven of eight patients with CCH on the interictal scans (Fig. 3), while diminished contralateral cerebellar perfusion was seen in the remaining patients (Fig. 4, Table 3).

DISCUSSION

CCD, a well-recognized SPECT finding in stroke patients, is generally considered to be secondary to a functional depression of a cerebellar hemisphere correlated with a contralateral cerebral lesion. This phenomenon results from a crossing of cortico-ponto cerebellar pathways and a functional connection between the contralateral cerebellar hemisphere and the cerebral cortex (*10,13,14*).

On the other hand, reversed condition (i.e., hyperperfusion or hypermetabolic state of a cerebellum) can occur due to the contralateral cerebral hemispheric hyperperfusion or hypermetabolism by the same mechanism. Indeed, Duncan et al. (*12*) reported a patient with focal epilepsy who had increased blood flow at the area of the epileptic focus accompanied by increased flow in the contralateral cerebellar hemisphere. They also observed that the hyperperfused ictal focus became slightly

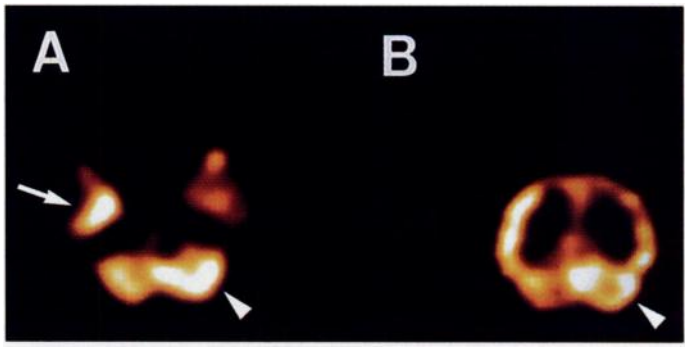

FIGURE 1. Right temporal epilepsy in a 30-yr-old woman. Ictal brain SPECT images demonstrate typical CCH. Transaxial (A) and coronal (B) images show increased uptake in the right temporal (arrow) and contralateral cerebellum (arrowhead).

TABLE 2
Location of Epileptic Foci and Incidence of CCH

Location	Epleptic focus	CCH
Rt. temporal	6	4
Lt. temporal	4	2
Rt. occipital	1	1
Lt. frontal	1	1
Total	12	8

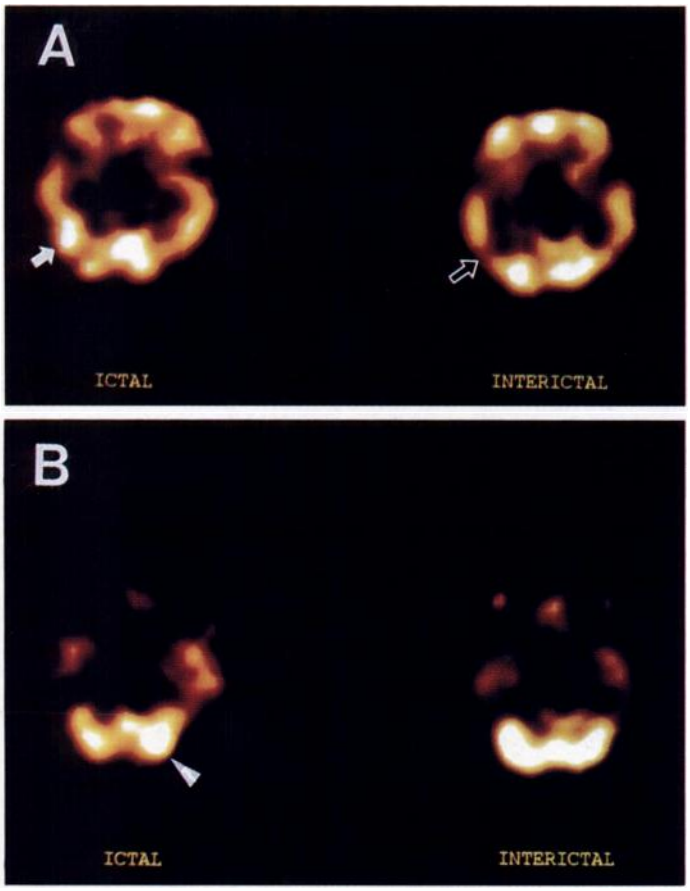

FIGURE 2. Right occipital lobe epilepsy in a 17-yr-old boy. (A) On ictal SPECT, there is subtle increased tracer uptake at the right occipital lobe (arrow). Interictal SPECT shows a focal area of decreased perfusion at the same site of the occipital lobe (open arrow). (B) Increased uptake of contralateral cerebellum (arrowhead) is more obvious than that of the occipital epileptic focus. Confirmation was made by ECoG with grid insertion. Interictal scan shows equalized cerebellar activity.

hypoperfused and cerebellar flow was symmetrically normalized on the interictal scan of the patient. Park et al. (*11*) also reported on a patient showing similar features in partial complex seizure related to the herpes simplex encephalitis. The

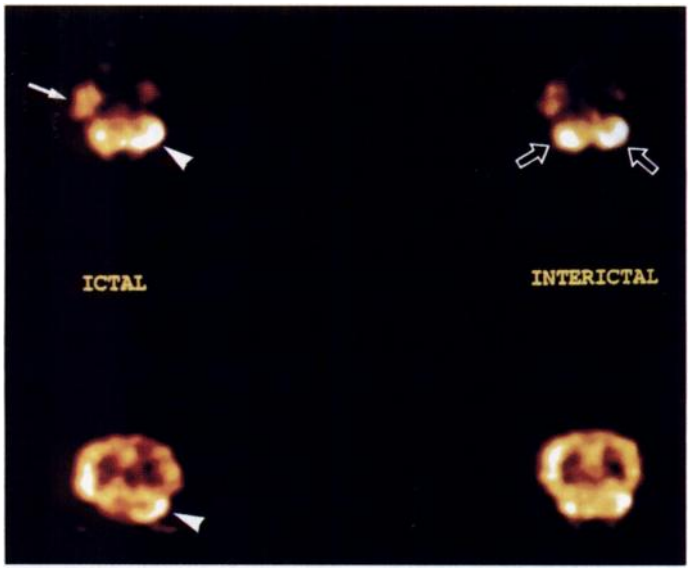

FIGURE 3. Right temporal lobe epilepsy in a 16-yr-old boy. Ictal SPECT shows increased uptake in right temporal lobe (arrow) and left cerebellar hemisphere (arrowhead). Interictal SPECT shows normal activity within the cerebellum (open arrows).

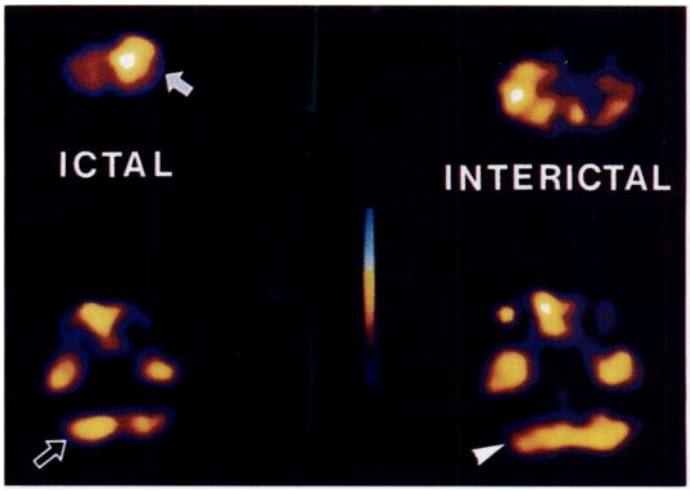

FIGURE 4. Left frontal lobe epilepsy in a 4-yr-old boy. Transaxial ictal SPECT shows increased uptake in left vertex (arrow) and right cerebellum (open arrow). Interictal SPECT demonstrates diminished uptake in epileptic focus and right cerebellum (arrowhead).

TABLE 3
Technetium-99m-HMPAO Activity of CCH Group on Interictal SPECT

Activity	Seizure foci	Contralateral cerebellum
Equalized	4	7
Decreased	4	1
Total	8	8

frequency or clinical usefullness of CCH in epilepsy, however, is not yet fully established. In this study, the frequency of CCH was 75% on ictal scans. CCH might therefore be described as a common finding on ictal brain SPECT in seizure patients. In two patients, the ictal scan showed almost normal uptake within the cerebral hemisphere but focal hot activity or diffusely increased uptake was seen within the contralateral cerebellum (Fig. 2). Surface EEG was not diagnostic. Follow-up interictal SPECT showed a focal area of decreased uptake in the right occipital region in one patient and in the right temporal lobe in the other which is contralateral to abnormal cerebellar uptake on the ictal scans. In the former patient, operative ECoG with grid insertion demonstrated abnormal focal wave at the right occipital area, which is concordant with the area seen as diminished activity on interictal SPECT. Therefore, CCH aided in the lateralization of seizure foci despite lack of typical uptake pattern on ictal SPECT or surface EEG.

CONCLUSION

CCH is a frequent finding of ictal brain SPECT in seizure patients and may aid in the lateralization of epileptic foci.

REFERENCES

1. Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised clinical and electroencephalographic classification of epileptic seizures. *Epilepsia* 1981;22:489–501.
2. Ojemann GA. Surgical therapy for medically intractable epilepsy. *J Neurosurg* 1987;66:489–499.
3. Kuzniecky R, Suggs S, Gaudier J, Faught E. Lateralization of epileptic foci by magnetic resonance imaging in temporal lobe epilepsy. *J Neuroimaging* 1991;1:163–167.
4. Engel J, Kuhl DE, Phelps ME, Rausch R, Nuwer M. Local cerebral metabolism during partial seizures. *Neurology* 1983;33:400–413.
5. Theodore WH, Newmark ME, Sato S, et al. Fluorine-18-fluorodeoxyglucose PET in refractory complex partial seizures. *Ann Neurol* 1983;14:429–437.
6. Devous MD Sr, Leroy RF, Homan RW. SPECT in epilepsy. *Semin Nucl Med* 1990;20:325–341.

7. Rowe CC, Berkovic SF, Sia STB, et al. Localization of epileptic foci with postictal SPECT. *Ann Neurol* 1989;26:660.
8. Lee BI, Markland ON, Wellman HN, et al. HIPDM-SPECT in patients with medically intractable complex partial seizures, ictal study. *Arch Neurol* 1988;45:397–402.
9. Shen W, Lee BI, Park HM, et al. HIPDM-SPECT brain imaging in the presurgical evaluation of patients with intractable seizures. *J Nucl Med* 1990;31:1280–1284.
10. Baron JC, Bousser MG, Comar D, Castaigne P. Crossed cerebellar diaschisis in human supratentorial infartion [Abstract]. *Ann Neurol* 1980;8:128.
11. Park CH, Kim SM, Streletz LJ, Zhang J, Intenzo C. Reverse crossed cerebellar diaschisis in partial complex seizures related to herpes simplex encephalitis. *Clin Nucl Med* 1992;17:732–735.
12. Duncan R, Patterson J, Bone I, Wyper DJ. Reversible cerebellar diaschisis in focal epilepsy. *Lancet* 1987;2:625–626.
13. Piero VD, Chollet F, Dolan RJ, Thomas DJ, Frackowiak R. The functional nature of cerebellar diaschisis. *Stroke* 1990;21:1365–1369.
14. Kurthen M, Reichmann K, Linke DB, et al. Crossed cerebellar diaschisis in intracarotid sodium amytal procedures: a SPECT study. *Acta Neurol Scand* 1990;81: 416–422.

Heterogeneity of Cerebral Hemodynamics and Metabolism in Carotid Artery Disease

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Methods: Eight patients with severe unilateral carotid stenosis (>70%) were evaluated using PET to assess parametric changes in cerebral blood flow, blood volume, metabolic rate for oxygen, metabolic rate for glucose, oxygen extraction fraction and glucose extraction fraction. We performed these examinations because clinical history and physical exam results suggested possible cerebral vascular disease. Four patients were neurologically asymptomatic with other signs of peripheral vascular disease (e.g., episodic vertigo, TIA and claudication). All patients had normal neurologic examinations and normal CT or MRI studies. PET images were analyzed by two methods. First, regions of interest were used for the entire hemisphere, vascular territories and borderzones. Regions ipsilateral to the carotid stenosis were compared to respective regions in the contralateral hemisphere using Student's t-test. Second, visual inspection of each image was performed. **Results:** Statistical analysis demonstrated no significant differences between hemodynamic and metabolic parameters for regions ipsilateral to the carotid stenosis and contralateral homotopic reference regions. Upon visual examination, however, all patients had focal changes in either cerebral blood flow, blood volume, glucose extraction fraction and/or oxygen extraction fraction. **Conclusion:** Visual inspection is important in the evaluation of pathophysiological changes caused by unilateral carotid stenosis. Clinical decisions in patients with carotid artery disease should be based on careful visual examinations and statistical analyses of appropriately selected regions.

Key Words: carotid artery disease; metabolism; cerebral blood flow; PET

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PET imaging of the brain continues to play an important role in the assessment of cerebrovascular disease. One of PET's many clinical uses is the evaluation of hemodynamically significant carotid artery disease for evidence of impaired cerebral blood circulation. This is a relatively crucial issue, since researchers hope to prevent the occurrence of a cerebrovascular accident and possible life-long disability by medical treatment or carotid endarterectomy.

A primary concern in this particular patient population is initial presentation. The results of investigations which examine the frequency of strokes as the first manifestation of hemodynamically significant carotid artery disease have been variable. Investigators report occurrence rates of stroke ranging from 0.6% to 19.1% in these patients (*1–3*). In clinical practice, it is generally believed that patients with hemodynamically significant carotid artery disease have an approximately 20%–30% chance of developing symptoms which by and large will be transient. There remains, however, a significant proportion of these patients who will probably present initially as a stroke without warning (*4*). Exploration of the hemodynamic status thus needs to be made as early as possible during the course of the disease. Since hemodynamic reserve and the effect of decreasing perfusion on tissue oxygen metabolism (*5*) can be assessed with PET, it has been used in an attempt to detect patients at risk. Several investigators, using the results of statistical region of interest (ROI) analysis, felt that the degree of carotid stenosis correlates poorly with the hemodynamic status of the ipsilateral cerebral circulation (*6–11*). Others claimed to have found a significant reduction of cerebral blood flow and hemodynamic reserve capacity in the borderzone regions between the anterior cerebral artery (ACA) and middle cerebral artery (MCA) ipsilateral to the carotid stenosis (*12,13*).

We present a PET study of eight patients with hemodynamically significant (>70%) unilateral carotid stenosis in whom the cerebral hemodynamic and metabolic status was evaluated. The following parameters were measured: cerebral metabolic rate for glucose (CMRgl), cerebral metabolic rate for oxygen ($CMRO_2$), oxygen extraction fraction (OEF), glucose extraction fraction (GEF), mean vascular transit time (MVTT), cerebral blood volume (CBV), cerebral blood flow (CBF) and cerebral metabolic ratio (CMR).

METHODS

Eight patients (5 men, 3 women; aged 56–70 yr, mean 64.5 ± 2.0 yr) with 70% or greater unilateral internal carotid artery stenosis were studied. Informed consent was obtained from all patients. Patients were referred for neurological assessment and Doppler sonography because of suspected cerebral vascular disease due to: (a) other signs of peripheral vascular disease (e.g., intermittent claudication, etc., n = 4), (b) episodic vertigo (n = 2), (c) transient ischemic attack (TIA) with mildly slurred speech (n = 1) and (d) nonspecific symptoms consisting of bilateral hand and foot paresthesias (n = 1). All patients had normal neurologic examinations and normal CT or MRI studies. The grade of stenosis was determined in all patients using carotid Doppler sonography. The study criterion was >70% unilateral carotid stenosis. Two patients had 70% stenosis, three patients had 80% stenosis and three patients had 90% stenosis.

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