Hemodynamic and Metabolic Effects of Cerebral Arteriovenous Malformations Studied by Positron Emission Tomography

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Seventeen patients with an intracranial arteriovenous malformation were studied with positron emission tomography. Cerebral blood flow, cerebral blood volume, oxygen extraction fraction, and glucose and oxygen metabolism were evaluated in both hemispheres, excluding the area of the malformation itself. Patients were divided into three groups according to the size of their malformation, and results obtained were compared with studies in healthy volunteers. The glucose metabolism was significantly \( p<0.01 \) decreased in the ipsilateral hemisphere in all patients. The cerebral blood volume was significantly increased \( p<0.001 \) ipsilaterally in the three groups, and contralaterally in patients with medium- and large-sized arteriovenous malformations. The cerebral blood volume to cerebral blood flow ratio, an index of vascular mean transit time, was significantly increased \( p<0.005 \) ipsilaterally in patients with medium- and large-sized malformations and contralaterally in patients with large ones. Cerebral blood flow, oxygen extraction fraction, and oxygen metabolism were within the normal range bilaterally in all three groups, but oxygen extraction fraction tended to be higher in patients with larger lesions. The lack of significant change in oxygen metabolism suggests that oxygen metabolism in cortical areas remote from the arteriovenous malformation has been maintained by compensatory hemodynamic mechanisms. These data reveal widespread metabolic and hemodynamic consequences of arteriovenous malformations and suggest that they are associated with impairment of glucose metabolism, both in ipsilateral regions remote from the lesion and in the contralateral hemisphere in patients with large lesions. (Stroke 1989;20:890–898)

Cerebral arteriovenous malformations (AVM) are relatively common lesions that produce seizures, intracranial hemorrhage, or progressive neurologic dysfunction.\(^1\)–\(^5\) They are characterized morphologically by the absence of resistance vessels between abnormal arteries and veins.\(^6\) The hemodynamic consequences of shunt flow through AVMs have been studied with intraoperative fluorescein angiography and krypton-85 clearance curve analysis,\(^7,8\) xenon-133 clearance,\(^9\) and isotope brain scanning.\(^10\) These and previous studies were restricted to the leptomeningeal circulation exposed at craniotomy, were limited by the reliability of the techniques employed, or were confined to measurements of cerebral blood flow (CBF). No study has addressed the metabolic consequences of AVMs or has correlated cerebral perfusion, metabolism, and hemodynamic compensatory mechanisms in these lesions.

Positron emission tomography (PET) is a noninvasive method of measuring CBF, cerebral blood volume, and the cerebral blood volume to cerebral blood flow ratio (mean vascular transit time), net extraction of oxygen, and cerebral oxygen and glucose metabolism in a tomographic fashion. Increases in cerebral blood volume in ischemic states are thought to result from dilatation of arterial resistance vessels in response to diminished cerebral perfusion pressure. The cerebral blood volume can be combined with CBF to produce the cerebral blood volume to cerebral blood flow ratio, an indicator of the mean time of transit of blood through the brain. A decrease of the reciprocal of this, the cerebral blood flow to cerebral blood volume ratio, has been shown to correlate well with increased oxygen extraction\(^11\) that may increase to as much as 90% in ischemia.\(^12\) In typical shunts, mean transit times and oxygen transfer would be...
expected to fall. In regions adjacent, mean transit times may rise because of lowered perfusion pressure; this prediction was confirmed in our study. We report the effects of cerebral AVMs on cerebral perfusion, metabolism, and hemodynamic and metabolic compensatory mechanisms in ipsilateral brain areas remote from the lesion and in the contralateral hemisphere in 17 patients.

Subjects and Methods

Subjects with angiographically confirmed supratentorial, intracerebral arteriovenous malformations were candidates for inclusion in our study. All subjects had complete medical histories and physical examinations recorded by a neurosurgeon or neurologist. Informed consent to participate in our study was given in all cases. At the time of the scans, no patient was being maintained on any drug therapy (sedative/hypnotic, antiepileptic) that would be expected to cause changes in cerebral metabolism.

Subjects were divided according to AVM size: lesions were graded according to the largest diameter of the nidus as seen on angiography. The arterial supply of the AVM was also noted on the angiograms.

Control values in volunteer subjects were used for comparison with the AVM patients because in this pathologic situation, with potentially bilateral effects of the AVM, the hemisphere contralateral to the malformation could not be assumed normal. Normal cerebral glucose metabolism values were obtained in 20 young control volunteers, 10 males and 10 females, with an age range of 18–32 years (mean 25 years). Cerebral blood flow, blood volume, oxygen extraction, and oxygen metabolism measurements were obtained in 11 young controls, four males and seven females, with an age range of 19–25 years (mean 22 years). All subjects except one glucose metabolism control were right-handed. Control studies were done under resting conditions with external stimulation kept to a minimum but without the use of earplugs or eye patches. Control subjects had no history of medical or neurologic diseases.

PET scans were collected on the Therascan 3128 positron tomograph, a two-ring scanner containing 64 bismuth germanate detectors per ring. Direct and cross-slice coincidences were acquired for three slices simultaneously. Image resolution was 12 mm (full width at half maximum) in the axial direction and in the transverse planes. Images were reconstructed using the Therascan standard software package, which includes a projection-thresholding procedure for analytic attenuation correction.

Patients were positioned in the scanner by means of a laser light aligned with the patients’ inferior orbito-meatal line. All oxygen-15 studies were done sequentially, without changing the patients’ position, and the position at the start and at the completion of each study was noted. For the fluorodeoxyglucose (FDG) study, the patient was positioned in the headholder in the same manner as for the oxygen-15 studies, with the laser aligned with the orbito-meatal line.

[15O]-labeled O2, CO2, and CO were administered sequentially in one session to provide three separate data sets. These were combined to provide functional maps for CBF, oxygen extraction fraction, and oxygen metabolic rate using the methodology of Frackowiak et al., and for cerebral blood volume, the method of Phelps et al. adapted for [15O]CO.

The [15O]O2 and [15O]CO2 gases were delivered continuously during the study. Labeled gases were mixed with 200 ml/min of medical air and were supplied to the patient through a plastic face mask. Once inhalation of the labeled gas was begun, equilibrium was established over a 10-minute period, followed by scans at the positions described for the FDG study. Typically, 1.5–2.5 million true events were recorded for each [15O]O2 image, and 2–4 million for each [15O]CO2 image.

[15O]CO was administered in a dose of 80 mCi/ml at 100 ml/min for 2–4 minutes. The [15O]CO supply was then discontinued and, after an equilibration period of 2 minutes, low-resolution images with a frame length of 3 minutes were obtained at the two scan positions. The low-resolution data acquisition mode used for the cerebral blood volume study was dictated by the tomograph design, the short tracer administration interval, and the fast radioactive decay of the label 15O. Typical images contained 300–500 thousand true coincidences.

Throughout these studies, blood samples were obtained for 15–20 seconds from an arterial line for the measurement of blood gases, whole blood, and plasma radioactivities. The oxygen analysis program generated a map for each of the four functional parameters (cerebral blood flow, cerebral blood volume, oxygen extraction fraction, and oxygen metabolism) for each anatomic plane as a composite data set. Oxygen extraction fraction and oxygen metabolism images were corrected for cerebral blood volume as described by Lammertsma et al., No blood volume correction was applied to the CBF values since, as shown by Lammertsma et al., a less than 4% overestimation in CBF would result from an arterial fraction as large as 30% of the total cerebral blood volume. Moreover, the functional values reported in this article were obtained from regions of interest that did not include the AVM per se.

F-labeled fluorodeoxyglucose was prepared on site; the specific activity was approximately 680 mCi/mmol. The patients received a 5-mCi bolus of FDG injected intravenously over 1 minute. 18F plasma activity and glucose concentration were measured from blood samples taken from the opposite arm using direct arterial sampling or sampling from an arterialized vein. Forty minutes after the injection of FDG, three tomographic slices were obtained simultaneously at each of two scan posi-
tions, encompassing the AVM site as well as distant cerebral tissue. The slice separation was 12 mm, and each set of three slices covered a brain section approximately 36 mm thick such that the two partially overlapping scan positions covered approximately 6 cm of cerebral tissue in the cephalocaudal direction. Between two and five million true coincidences were obtained per slice in these static scans.

The analysis of the static FDG scans was based on the Phelps et al.23 adaptation of the Sokoloff et al method.24 In addition, a reformulation of the operational equation suggested by Brooks was incorporated.25 The values of the lumped constant and the FDG rate constants used were those established by Huang et al.26

Because of the difficulties in quantification within the AVM and since this study was aimed at the evaluation of effects on surrounding and remote tissue, no values are reported from the malformations themselves.

Metabolic and hemodynamic PET studies were analyzed by placing circular regions of interest 9 mm in diameter over areas of the cortical gray matter, caudate, thalamus, and lentiform nucleus, which were not involved in the AVM itself. The same x, y, z spatial coordinates were used for region of interest placement on all studies. Results were grouped according to size of the AVM and represent the hemispheric means of all regions, excluding the area of the AVM. In analyzing each PET cross-sectional slice, approximately six to eight different regions of interest were placed over the contralateral hemisphere, and four were placed over the ipsilateral hemisphere excluding the area of the AVM itself. Individual regions-of-interest values in each hemisphere were then averaged to obtain mean values ±SD.
TABLE 1. Patient Population

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Location</th>
<th>AVM size</th>
<th>Major vascular supply</th>
<th>Angiographic steal phenomenon</th>
<th>CT evidence of hemorrhage</th>
<th>Seizures</th>
<th>Symptom signs</th>
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<td>L</td>
<td>MC, AC</td>
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AVM, arteriovenous malformation; CT, computed tomography; ACo, anterior communicating artery; PCo, posterior communicating artery; S, small (<6 cm); MC, middle cerebral artery; PC, posterior cerebral; F, focal motor; GTC, generalized tonic-clonic; AC, anterior cerebral; I, angiograms obtained insufficient to determine presence or absence of steal phenomenon; OBS, organic brain syndrome; D, dysphasia; M, medium (>6–11 cm); HP, hemiparesis; HA, headache; HH, homonymous hemianopsia; L, large (>11 cm).

Analyses of variance (ANOVA) were carried out with the individual hemispheric means for CBF, cerebral blood volume, oxygen extraction fraction, oxygen metabolic rate, glucose metabolism, and CT evidence of hemorrhage.

FIGURE 1. Positron emission tomography (Patient 5, Table 1). Opposite page, top left: Marked ipsilateral and moderate contralateral decrease in cerebral glucose metabolism. Top right: Decrease in cerebral blood flow ipsilateral to arteriovenous malformation (AVM). Opposite page, bottom left: Oxygen extraction. Bottom right: Increased cerebral blood volume ipsilaterally. This page, left: Marked global decrease in cerebral oxygen metabolism that is more pronounced in area of medium-sized left temporoparietal AVM seen on computed tomography scan (right). (Nota bene: AVM was in left hemisphere, which is left in all six images.)
cerebral blood volume to cerebral blood flow ratio, respectively, as the dependent variables and AVM size (small, medium, large) and side of lesion (ipsilateral, contralateral) as factors.

Results obtained in the AVM patients were compared with the normal control results by means of a Student’s t test, and a patient value differing more than 2 standard deviations from the mean control value was judged abnormal. In addition, linear regression analysis was applied to the results to determine the presence of significant correlations of metabolic values depending on AVM size and to determine possible correlations between metabolic and hemodynamic values themselves.

Results

Eight males and nine females aged 18 to 62 years (mean±SD, 33.0±11.8 years) underwent PET studies for the investigation of an intracranial AVM (Table 1). Twelve patients had a seizure disorder, two had suffered a remote intracranial hemorrhage, and three had sustained an intracranial hemorrhage within 1 to 3 months before PET scanning. None had undergone treatment for their AVM before the PET studies.

On angiography, the AVMs were supplied by the middle cerebral artery in all 17 cases. In addition there was supply to the AVM from the anterior cerebral artery in six cases, and from the posterior cerebral artery in four cases. Collateral supply to the AVM from the contralateral carotid circulation or from the vertebrobasilar system through the anterior communicating and posterior communicating arteries respectively was observed on angiography in 12 patients (Table 1). Angiography was insufficient to assess supply from the contralateral anterior communicating artery in five cases and from the posterior communicating artery in three cases.

There were four lesions ≤6 cm (small), 10 lesions >6–11 cm (medium), and three >11 cm (large). Most lesions >6 cm received a portion of their blood supply across the midline through the communicating artery. The locations of the AVMs are shown in Table 1.

Four patients were mildly hemiparetic, two were hemiplegic, two had an homonymous hemianopsia, two were dysphasic, and one had an organic brain syndrome. Six patients had a normal neurologic examination.

PET Data. Because of technical difficulties, satisfactory studies were not obtained for cerebral glucose metabolism in three cases (8, 12, 13), for CBV in three cases (8, 1, 3), and for oxygen extraction and oxygen metabolism in two cases (1, 3).

The hemodynamic and metabolic parameters for the hemispheres ipsilateral and contralateral to the AVM were grouped according to the size of the AVM and were compared with control values. Images from a typical patient (5, Table 1) are presented in Figure 1. The only significant finding revealed by the ANOVAs was a main effect of side for cerebral blood volume (F_{1,11}=25.5; p<0.001) and cerebral blood volume to blood flow ratio (F_{1,11}=12.9; p<0.01); that is, cerebral blood volume and cerebral blood volume to blood flow ratio were significantly increased ipsilaterally as compared with those of the opposite side in the same subject, regardless of lesion size as indicated by the absence of any significant interactions with the AVM size factor. Results are shown in Table 2 for cerebral glucose metabolism, oxygen extraction fraction, cerebral blood volume, and blood volume to blood flow ratio. Results more than ±2 standard deviations from control values were noted, and the level of significance is given. In no group was CBF or cerebral oxygen metabolism significantly decreased, nor was oxygen extraction significantly increased relative to control values. Cerebral blood volume was significantly increased (p<0.001) with respect to control values in all areas except for contralateral regions in patients with small AVM. Changes in cerebral blood volume to cerebral blood flow ratio were not matched by significant changes in cerebral oxygen extraction, although there was a trend toward rising oxygen extraction fraction with increasing cerebral blood volume to cerebral blood flow values.

Abnormal cerebral glucose metabolism results in individual patients did not correlate with the presence of a seizure disorder or with a history of intracranial hemorrhage. In the five patients with histories of intracranial hemorrhage, two had normal glucose metabolism bilaterally (3 and 7, mean glucose metabolism=49.1±11.2 and 53.7±6.9 μmol/100 g/min, respectively), with only a tendency for lower ipsilateral glucose metabolism. One patient had decreased cerebral glucose metabolism bilaterally (15, mean glucose metabolism=30.9±1.2 μmol/100 g/min), and one had decreased glucose metabolism ipsilaterally only (14, glucose metabolism=20.3±3.8 μmol/100 g/min ipsilateral, 54.9±18 μmol/100 g/min contralateral). In the other case (8), cerebral glucose metabolism measurements were not obtained for technical reasons. It should be noted that in the control population, no significant difference was noted between cerebral glucose metabolism values obtained from studies using arterialized venous blood samples and those using direct arterial sampling.27

Hemodynamic and metabolic parameters were examined for the individual patients. Ipsilateral to the AVM, a significant (>2 SD from normal) hemispheric decrease with respect to the control population was noted in 50% of patients in cerebral glucose metabolism, in 18% of patients in CBF, and in 13% in cerebral oxygen metabolism. Contralaterally, 36% of patients had a decrease in cerebral glucose metabolism, 6% had a decrease in CBF, and none had a decrease in cerebral oxygen metabolism. The cerebral blood volume to cerebral blood flow ratio was calculated as an index of mean transit time; results in the ipsilateral and contralateral...
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Table 2. Metabolic and Hemodynamic Parameters (Mean±SD) Ipsilateral and Contralateral to the AVM, by AVM Size

<table>
<thead>
<tr>
<th></th>
<th>LCMRGL (μmol/100 g/min)</th>
<th>CBF (ml/100 g/min)</th>
<th>CBV (ml/100 g)</th>
<th>OEF (%)</th>
<th>CMRO2 (μmol/100 g/min)</th>
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<td>Ipsilateral</td>
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<tr>
<td>Small</td>
<td>35.2±7.6</td>
<td>54.4±16.0</td>
<td>7.6±0.8</td>
<td>0.34±0.08</td>
<td>180.0±19.6</td>
</tr>
<tr>
<td>(p&lt;0.01)</td>
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<tr>
<td>Medium</td>
<td>33.7±13.4</td>
<td>44.3±22.1</td>
<td>11.4±3.0</td>
<td>0.44±0.07</td>
<td>164.7±74.1</td>
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<tr>
<td>(p&lt;0.005)</td>
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<tr>
<td>Large</td>
<td>29.7±6.8</td>
<td>45.2±19.2</td>
<td>11.9±5.1</td>
<td>0.52±0.08</td>
<td>174.0±8.6</td>
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<td>(p&lt;0.001)</td>
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<td>Contralateral</td>
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<tr>
<td>Small</td>
<td>39.5±13.0</td>
<td>51.1±15.6</td>
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<td>170.8±43.1</td>
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<td>(p&lt;0.05)</td>
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<tr>
<td>Medium</td>
<td>42.5±12.8</td>
<td>48.1±20.6</td>
<td>5.5±1.8</td>
<td>0.42±0.08</td>
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<td>(p&lt;0.001)</td>
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<tr>
<td>Large</td>
<td>36.0±5.5</td>
<td>38.6±11.3</td>
<td>8.2±2.5</td>
<td>0.48±0.07</td>
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<td>(p&lt;0.01)</td>
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<tr>
<td>Global mean</td>
<td>47±7</td>
<td>49±12</td>
<td>4.3±0.2</td>
<td>0.42±0.08</td>
<td>178±44</td>
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p values denote level of t test significance between patients’ mean values and controls’ mean values. AVM, arteriovenous malformation; LCMRGL, glucose metabolism; CBF, cerebral blood flow; CBV, cerebral blood volume; OEF, oxygen extraction fraction; CMRO2, oxygen metabolism.

Discussion

Cerebral AVM are detrimental to the brain in many ways: they are the third major cause of spontaneous intracranial hemorrhage, they often
serve as epileptogenic foci producing cerebral seizures,28 and they cause progressive neurologic deficits, presumably from chronic low-grade cerebral ischemia.2-4 Although shunts may reduce perfusion pressure sufficiently to create the "cerebral steal syndrome,"27,28 little quantitative information on the hemodynamic or metabolic effects of AVMs in general is available. Our study of 17 patients with supratentorial AVMs describes the changes in cerebral perfusion and metabolism that may be produced by these lesions.

The validity of the oxygen-15 steady-state model in the presence of AVMs has been discussed by Lammertsma et al.24 Apart from the fact that we do not report any functional parameters from the AVM regions per se, the analysis of these authors indicates that regional cerebral blood flow (rCBF) values not corrected for cerebral blood volume only minimally overestimate (4%) true rCBF for regions with feeding arterial channels representing up to 30% of the total blood volume in a selected region of interest. If the arterial blood volume is assumed negligible (i.e., all blood volume is considered venous), the steady-state model does not require any cerebral blood volume correction. No blood volume correction was therefore applied to the CBF values presented here. The oxygen extraction values were, however, properly corrected for oxygen-15 activity in the vascular space as described in References 20 and 21 since the uncorrected value significantly overestimates (>10%) the true extraction fraction of oxygen.

Our hemodynamic and metabolic studies using PET help to further quantify the effects of cerebral AVMs both in the ipsilateral hemisphere and contralaterally. Our data indicate a consistent increase in ipsilateral cerebral blood volume and blood volume to blood flow values as compared with those of the opposite side in all subjects regardless of lesion size. Also, the ipsilateral blood volume to blood flow ratio is significantly higher than normal in patients with an AVM and is proportional to the size of the lesion (Table 3). Mild CBF changes were noted in the ipsilateral cortex remote from the AVM and in the contralateral hemisphere, but these changes did not achieve statistical significance. In isolation, CBF has been shown to be a poor indicator of the adequacy of cerebral perfusion relative to the metabolic needs of the tissue. For example, in the late phase of stroke, CBF can be markedly increased in regions where metabolic needs have been depressed,30 while in the initial phase of stroke, CBF is decreased and oxygen extraction increased.21,32

Despite the fact that cerebral blood volume does not directly supply information on the metabolic state of the brain, cerebral blood volume, especially when combined with CBF in a ratio, may be a more reliable indicator of the hemodynamic state.11 In cerebral ischemia, with diminished cerebral perfusion pressure, blood volume most likely increases because the small resistance vessels that maintain blood flow dilate.33 However, the increase in cerebral blood volume could also be due to dilatation of capacitance vessels in response to increased venous pressure. Cerebral blood volume increases remote from the AVM occurred ipsilaterally in all cases and contralaterally in 50%. This indicates that the ipsilateral cortex remote from the AVM, and the contralateral cortex in many cases, were exposed to lowered perfusion pressure because of diversion of blood through the arteriovenous fistula. The increased cerebral blood volume did not completely compensate for the reduced cerebral perfusion pressure in all cases, however, as evidenced by a tendency toward a rising oxygen extraction. Thus, although a "steal" of blood flow was not documented and CBF was maintained, a type of "steal" phenomena, while compensated, did exist in the decreased perfusion pressure seen.

The intracerebral steal phenomenon has been most convincingly demonstrated by intraoperative fluorescein angiography and microregional cerebral blood flow analysis at the time of craniotomy for resection of AVMs.7,8 Using these techniques, Feindel and coworkers7 were able to characterize the intracerebral steal syndrome as it affects the hemisphere ipsilateral to the AVM. They demonstrated conclusively that large cerebral AVMs can adversely affect cerebral perfusion at a distance in the ipsilateral cerebral hemisphere, which may account for the development of progressive symptoms and signs such as progressive sensory or motor deficits or mental deterioration associated with large AVMs. Olivecrona and Rieves appreciated that cerebral AVMs have hemodynamic effects on the contralateral hemisphere when they saw filling of the lesions with contralateral carotid angiography. Such interhemispheric stealing of blood has been correlated to electroencephalogram (EEG) abnormalities in the hemisphere contralateral to the lesion.24,25 Similarly, contralateral CBF changes have been observed with single-photon emission computed tomography in some patients with AVMs.26

From a metabolic viewpoint, our data show that mean oxygen extraction fraction tends to increase bilaterally with increasing size of the AVM and increasing mean transit time, although these values were less than 2 standard deviations from normal. Mean group values for cerebral oxygen metabolism were not significantly different from normal nor did they correlate with the size of the AVM; nevertheless, individual cases showed significantly decreased oxygen metabolism. This was seen in conjunction with a significant ipsilateral decrease in glucose metabolism in all groups and a contralateral decrease in 36% of patients. The oxygen metabolism may in fact be affected by the presence of the AVMs in more cases, but this effect may be difficult to detect with statistical significance because of the variability seen in these measurements. Decreases in glucose metabolism without similar changes in oxygen
metabolism may also suggest that alternate substrates are being used in these cases. With regard to possible methodologic artifacts that could explain this result, it should be noted that for the control population (Table 1), the coefficient of variation for oxygen metabolism, which is a derived quantity (oxygen extraction×CBF) is almost twice as large as that for glucose metabolism. For a given sample size, the same percentage change in the two parameters, therefore, might turn out to be statistically significant for cerebral glucose metabolism but not for oxygen metabolism. Methodologic problems exist with the quantification of glucose metabolism in pathologic states such as severe ischemia. Since severe ischemia was not present in our cases, the rate constants and lumped constant used were those of normal brain. No significant cerebral edema was seen, and no midline shifts were noted on CT scans to explain contralateral or ipsilateral mass effect changes. Similarly, hemodynamic abnormalities might be expected in areas of the contralateral hemisphere affected by a cerebral "steal" phenomenon. The changes observed in these parameters cannot be attributed to conditions other than the presence of the AVM itself. For example, although seizure disorders are known to cause decreased glucose metabolism, the presence of seizure disorders or antiepileptic therapy in some patients probably was not responsible alone for the decreased cerebral glucose metabolism seen. The presence of isolated focal seizure disorders in seven patients might explain focal or diffuse changes in cerebral glucose metabolism, but generalized seizures would not necessarily produce significant interictal effects on glucose metabolism. In all, decreased cerebral glucose metabolism was seen in only six of the 10 epileptic patients who had FDG scans performed. Also, two patients with large AVMs and significant abnormalities in all parameters studied had no seizures. Similarly, the history of intracranial hemorrhage in five patients might have contributed to a depression of their cerebral glucose metabolism, but such abnormalities were also seen in the 12 patients without hemorrhage, and the history of hemorrhage did not correlate with the degree of functional impairment in the patients.

AVMs may increase in size with increasing age, which can lead to increased diversion of nutritional flow away from normal brain, producing progressive neurologic deterioration or dementia. Our data indicate that the presence of an AVM may be detrimental to ipsilateral brain remote from the lesion and to the contralateral hemisphere as evidenced by decreased glucose metabolism and increased cerebral blood volume. The cerebral blood volume to cerebral blood flow ratio correlates well with progressively increasing size of the AVMs. This correlation suggests that those cases with large-sized AVMs, compared with small AVMs, are in a more precarious hemodynamic/metabolic balance. These parameters may therefore prove to be useful criteria, aiding in the evaluation of patients with AVMs.

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References

12. Wise RJS, Bernardi S, Frackowiak RSJ, Legg NJ, Jones T: Serial observations on the pathophysiology of acute stroke. The transition from ischemia to infarction as reflected in regional oxygen extraction. Brain 1983;106:197–222
34. Loeb C, Favale E: Contralateral EEG abnormalities in intracranial arteriovenous aneurysms. Arch Neurol 1962; 17:121-128
40. Metter EJ, Jackson C, Kempler D, Riegel WH, Hanson WR, Mazziootta JC, Phelps ME: Left hemisphere intracerebral hemorrhages studied by (F-18)-fluorodeoxyglucose PET. Neurology 1986;36:1155-1162

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