Changes of Blood Flow in the Cerebral Cortex
After Subcortical Ischemic Infarction

Else Højjer-Pedersen, MD, and Ole Fritz Petersen, MD

The two-dimensional xenon-133 inhalation method was used to measure cortical blood flow in 16 patients with small subcortical ischemic infarcts and in 10 patients with larger cortical infarcts in the chronic phase of stroke. An abnormal hemispheric asymmetry of blood flow was seen, not only in patients with cortical infarcts, but also in those with subcortical infarcts. In the patients with subcortical infarcts, focal areas of reduced cortical blood flow were seen in the symptomatic hemisphere remote from the tissue destruction, usually including part of the noninfarcted frontoparietal cortex. The cortical dysfunction may have contributed to the clinical manifestations including aphasia, which was present in 14 of the 16 patients with subcortical lesions. (Stroke 1989;20:211-216)

Measurements of regional cerebral blood flow (rCBF) with the two-dimensional xenon-133 inhalation technique, calculated as the initial slope index (ISI), reveal the perfusion in the outermost part of the brain, mainly the cortex. Minor infarcts situated deep in the brain, with no cortical extension and covered by a layer of apparently normal brain parenchyma, may be expected not to influence the rCBF findings. To test this suggestion, we analyzed the results of rCBF measurements as to global and focal changes in a group of patients with subcortical infarcts and compared the rCBF findings with those in a group of patients with cortical infarcts and in a group of controls. rCBF was measured during the chronic phase of stroke, when the changes of blood flow have stabilized and the uncoupling of cerebral blood flow and metabolism seen in the acute postinfarct period has disappeared.

Subjects and Methods

Our study comprised 26 patients with symptoms of unilateral cerebral ischemia in the carotid territory. We included only patients in whom computed tomography (CT) confirmed the presence of non-hemorrhagic cerebral infarcts. Sixteen patients had deep cerebral infarcts without cortical involvement (Figure 1); in the remaining 10 patients the infarcts affected the cortex and underlying structures (Figure 2). The size of the infarcts was estimated by multiplying the length by the width of the hypodense lesion in the slice showing the largest area. This product was multiplied by the depth, summed across the several slices showing the lesion. The size of the infarcts is indicated in Table 1. CT scanning was performed using third-generation scanners a mean of 46 (range 4-216) days after the onset of the ischemic symptoms.

Table 1 summarizes the patient data and clinical findings. Fifteen of the 16 patients with subcortical infarcts had left hemisphere lesions, and among the 15, 14 were aphasic in the acute stage. All 16 patients with subcortical stroke were right-handed; three had hypertension. The clinical evaluation in the chronic stage took place when rCBF was measured, a mean of 113 (range 27-228) days after the onset of the symptoms. At that time all 26 patients were independent in activities of daily living.

We also measured rCBF in 23 normal healthy volunteers (controls) after informed consent was obtained. The volunteers were 29–70 (mean 51) years old and had no brain disorders, hypertension, or diabetes by history.

rCBF was measured in both patients and controls using the xenon-133 inhalation technique on a Novo Cerebrograph with 16 scintillation detectors for each side of the head, with the collimator tubes perpendicular to the brain surface. The system has been described in detail elsewhere. During the measurements the subjects were lying in a quiet room, resting, with their eyes covered and their ears plugged. Paco₂ was estimated from recordings on a capnograph of end-tidal CO₂ concentrations during the investigations and was found to be
The rCBF data were analyzed as to hemispheric asymmetry and focal abnormalities. Hemispheric asymmetry was quantified as the difference between the mean hemispheric ISI values in the asymptomatic and symptomatic hemispheres. Focal changes were defined as ISI values of two or more adjacent detectors in a hemisphere differing from the ISI values of the corresponding detectors in the other hemisphere by >7.2%, a difference that was not exceeded in any of the 23 controls in this study. The absolute hemispheric rCBF values were not evaluated because of the variability with age and other physiologic conditions.

Statistical analyses were performed with the paired and unpaired t tests.

**Results**

**Controls**

rCBF in the two hemispheres was almost identical, in accordance with other investigations; the difference between the right and left mean hemispheric ISI values was nonsignificant (mean difference 0.1, SD 0.7, p<0.3), which means that a hemispheric difference of ±1.5 is abnormal with a confidence level of <5%. rCBF values were correlated with age, and a significant decline of blood flow with advancing age was found, as has been reported previously and in accordance with other studies. Therefore, our results in these controls were considered to be representative of normality.

**Patients With Subcortical Infarcts**

Hemispheric asymmetry ranged from -0.9 to 4.2 (mean 1.6, SD 1.5) (Table 2); the mean difference between hemispheres was highly significant (p<0.005). The greatest hemispheric asymmetries appeared in four of the five patients with the largest lesions on CT. This tendency of increasing hemispheric asymmetry with increasing infarct size was not analyzed statistically because of the small number of patients and the inexactness of infarct size measurements.

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**Figure 1.** Schematic representation of appearance on computed tomogram of subcortical infarcts in 16 patients in ascending order of size of infarct cavity. Slice with largest lesion is shown. Patient number beneath each slice.

**Figure 2.** Schematic representation of appearance on computed tomogram of cortical infarcts in 10 patients in ascending order of size of infarct cavity. Slice with largest lesion is shown. In Patients 24 and 30, slices nearer top of head showed cortical involvement. Patient number beneath each slice.
Fourteen patients had focal areas of decreased rCBF in the symptomatic hemisphere, usually involving at least part of the frontal region (Table 2, Figure 3). As seen in Figure 1, no infarct in these patients affected the frontal cortex.

In two of these 14 patients an ipsilateral focal area with increased rCBF was also seen. In Patient 3 a small temporop-occipital area was localized adjacent to the frontal low-flow area, which presented an ISI value 10.3% higher than that of the corresponding area in the asymptomatic hemisphere. In Patient 5 a frontal area adjacent to the frontoparietal low-flow area had an ISI value 7.5% higher than that on the other side. In both patients the rCBF examinations were performed >2 months after the stroke, and the patients were clinically stable. They appeared slightly demented, being slow, with difficulties in concentrating and memorizing. Patient 3 had been healthy previously, whereas Patient 5 suffered multiple transient ischemic attacks (TIAs) before his stroke.
TABLE 2. Cortical Blood Flow in 26 Patients With Symptoms of Unilateral Cerebral Ischemia

<table>
<thead>
<tr>
<th>Pt</th>
<th>Hemispheric asymmetry</th>
<th>Focal low-flow area in symptomatic hemisphere</th>
<th>Focal % difference in low-flow area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.3</td>
<td>Frontal and temporal</td>
<td>10.7</td>
</tr>
<tr>
<td>2</td>
<td>1.6</td>
<td>Frontal and parietal</td>
<td>9.5</td>
</tr>
<tr>
<td>3</td>
<td>0.4</td>
<td>Frontal</td>
<td>10.4</td>
</tr>
<tr>
<td>4</td>
<td>2.0</td>
<td>Frontal</td>
<td>15.3</td>
</tr>
<tr>
<td>5</td>
<td>0.4</td>
<td>Frontoparietal</td>
<td>9.1</td>
</tr>
<tr>
<td>6</td>
<td>0.9</td>
<td>Frontal</td>
<td>12.0</td>
</tr>
<tr>
<td>7</td>
<td>−0.6</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>0.2</td>
<td>Parieto-occipital</td>
<td>7.5</td>
</tr>
<tr>
<td>9</td>
<td>1.6</td>
<td>Frontal and parietal</td>
<td>12.0</td>
</tr>
<tr>
<td>10</td>
<td>0.8</td>
<td>Frontotemporal</td>
<td>14.6</td>
</tr>
<tr>
<td>11</td>
<td>1.3</td>
<td>Frontoparietal</td>
<td>16.2</td>
</tr>
<tr>
<td>12</td>
<td>4.2</td>
<td>Frontal and parieto-occipital</td>
<td>14.1</td>
</tr>
<tr>
<td>13</td>
<td>3.4</td>
<td>Frontoparietal</td>
<td>14.1</td>
</tr>
<tr>
<td>14</td>
<td>3.9</td>
<td>Frontotemporal and parietal</td>
<td>18.5</td>
</tr>
<tr>
<td>15</td>
<td>−0.9</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>3.9</td>
<td>Frontotemporo-occipital</td>
<td>16.2</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>1.6±1.5*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Cortical infarcts

<table>
<thead>
<tr>
<th>Pt</th>
<th>Focal low-flow area in symptomatic hemisphere</th>
<th>Focal % difference in low-flow area</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>1.4 Frontal and temporoparietal</td>
<td>8.6</td>
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<tr>
<td>22</td>
<td>3.5 Frontoparietal</td>
<td>14.8</td>
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<tr>
<td>23</td>
<td>0.8 Frontotemporal</td>
<td>11.7</td>
</tr>
<tr>
<td>24</td>
<td>1.3 Frontoparietal</td>
<td>12.0</td>
</tr>
<tr>
<td>25</td>
<td>2.4 Frontal and temporoparietal</td>
<td>13.2</td>
</tr>
<tr>
<td>26</td>
<td>2.3 Temporoparieto-occipital</td>
<td>16.7</td>
</tr>
<tr>
<td>27</td>
<td>2.8 Frontoparietal</td>
<td>16.2</td>
</tr>
<tr>
<td>28</td>
<td>0.8 Frontal and parietal</td>
<td>14.2</td>
</tr>
<tr>
<td>29</td>
<td>3.3 Frontotemporo-occipital</td>
<td>16.5</td>
</tr>
<tr>
<td>30</td>
<td>1.6 Frontoparietal</td>
<td>11.7</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>2.0±1.0†</td>
<td></td>
</tr>
</tbody>
</table>

Hemispheric asymmetry, initial slope index of asymptomatic hemisphere minus that of symptomatic hemisphere.

*1p<0.005, 1p<0.001, significant difference between hemispheres by paired t test.

In Patients 7 and 15 no focal abnormalities were present, and the differences of ISI between hemispheres were within the limits seen in the controls.

Patients With Cortical Infarcts

Hemispheric asymmetry was present, with the lower ISI in the symptomatic hemisphere. The difference between hemispheres ranged from 0.8 to 3.5 (Table 2); the mean difference (2.0±1.0) was highly significant (p<0.001). Hemispheric asymmetry tended to be more pronounced than with subcortical infarcts; however, this was not significant (p<0.4).

Focal areas of reduced rCBF in the symptomatic hemisphere were observed in all 10 patients (Table 2), and two typical cases are illustrated in Figure 3. Comparison of the blood flow maps and the CT scans revealed consistent changes on the whole.

In Patients 23 and 28 the blood flow maps showed, adjacent to the low-flow areas, focal areas with increased rCBF compared with the asymptomatic hemisphere. In Patient 23 an area with 16.7% higher ISI was localized in the occipital region, and in Patient 28 an area with 10.4% higher ISI was seen frontal to the frontal and parietal low-flow area. The rCBF assessments had been performed >2 months after the stroke, at a time when the patients had made a good recovery and did not appear demented. Patient 23 had been healthy previously, whereas Patient 28 had one TIA 16 months before his stroke.

Discussion

Our results suggest that subcortical infarction causes significant hemispheric asymmetry of blood flow in the cerebral cortex as measured by the two-dimensional xenon-133 inhalation method after the acute stage of stroke. Hemispheric asymmetry appeared to be of the same magnitude as that seen in cortical infarcts, although subcortical infarcts were smaller. Remote focal areas of decreased rCBF in the ipsilateral cortex, predominantly in the frontoparietal region, were present with the subcortical infarcts in 14 of 16 patients.

Distant reductions of rCBF (diaschisis) have been described in acute stroke in studies performed before the introduction of CT.16-22 Only a few studies report the influence of discrete subcortical infarcts on rCBF recorded by the two-dimensional clearance technique in chronic stroke. Takano et al23 studied the effect of small, deep hemispheric infarcts in the subacute-chronic stage on the ipsilateral cortical circulation using the xenon-133 intracarotid injection technique; a focal area of hypoperfusion around the central sulcus was observed in all 10 patients studied, whereas no information was given on hemispheric asymmetry due to the method used. In another study24 using the xenon-133 intracarotid injection technique, rCBF was recorded in 10
patients with subcortical lesions on CT, and large low-flow areas were observed in five patients, whereas rCBF was normal in the other five; however, the recordings were performed in the acute stage, an average of 2 days after the stroke, in contrast to the chronic static lesions in our study.

Three-dimensional methods based on positron emission tomography (PET) have shown an area of depressed rCBF larger than that of the anatomic infarct on CT. Remote effects were noted in both the acute and the chronic postinfarction periods. In patients with lacunar infarcts in the internal capsule or the basal ganglia, PET images showed decreased rCBF in the frontoparietal cortex ipsilateral to the lesion. Decreased rCBF in chronic lesions was coupled with decreased rate of metabolism. In unilateral chronic vascular thalamic lesions, a significant metabolic hemispheric asymmetry at the expense of the affected side has been demonstrated, and furthermore, a tendency of a regional pattern of cortical hypometabolism was observed. A reduction in blood flow matched that in metabolism. Our findings, obtained with much less advanced equipment, appear to support the PET results. A study using single-photon emission computed tomography (SPECT) in a series of 16 patients with unilateral subcortical hemorrhagic or ischemic stroke demonstrated a significantly greater reduction of cortical blood flow in eight patients with aphasia and neglect than in eight patients without neuropsychological deficits. rCBF in that study was measured both during a very acute phase (≤24 hours) and up to 33 (average 15) days after the stroke in contrast to our study in which we measured rCBF not earlier than 27 (mean 113) days after the onset of symptoms. The different time schedule makes comparison of the rCBF results in the two studies difficult due to changes of rCBF from the acute to the chronic phase in stroke. However, a concordant finding was cortical hyperperfusion in patients with aphasia and subcortical infarcts.

In addition to focal areas of low rCBF, focal areas of relatively increased rCBF were seen in four of our 26 patients. Areas of increased blood flow, luxury perfusion, and relative or absolute hyperemia have been described in acute stroke. However, our patients were in a chronic phase after stroke, without any clinical evidence of deterioration at the time rCBF was measured. The focal areas gave a spotty appearance to the blood flow maps, as with multi-infarct dementia. Two of the four patients were slightly demented but the other two were not. It appears difficult to draw any firm conclusion from our data on these four patients.

CT findings in cerebrovascular disease have been correlated with neuropathologic findings, and it was very difficult to detect accurately on CT small infarcts of <5 mm largely because of the limitations in the efficiency of the CT scanner. Therefore, independent small infarcts in the cortex may have been present in our patients, contributing to the rCBF abnormalities in subcortical lesions. However, it appears that this alone may not explain our findings of a hemispheric asymmetry of the same magnitude in these patients as in the patients with rather large cortical infarcts.

Several reports have been published recently on the clinical effects of subcortical stroke on “higher cortical functions” such as language, cognition, praxic functions, and aphasia; cognitive deficits and apraxia have been described in deep cerebral lesions. Fourteen of our 16 patients with subcortical infarcts were aphasic in the acute stage. Several mechanisms responsible for the observed symptoms have been proposed in the literature: compression of adjacent structures, disconnection of strategic efferent and afferent fiber tracts of the cortex, and damage to basal ganglia gray matter; reduction of cortical blood flow and metabolism may contribute, also. It is unknown if these changes are secondary to deafferentation, with adjustment of blood flow to reduced metabolic activity. However, these changes do show that the cortex is involved and dysfunctional in subcortical tissue destruction, which may explain why some clinical manifestations resembled cortical symptoms. In some of our patients blood flow abnormalities were present after the symptoms had disappeared, which may mean that rCBF measurements give more subtle information on regional function than clinical evaluation and may demonstrate the complexity of clinical recovery. Further studies may give important information on pathophysiology and recovery in subcortical stroke.

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