Relation of Cerebral Blood Flow to Motor and Cognitive Functions in Chronic Stroke Patients

Sakan Mori, MD; Seizo Sadoshima, MD; Setsuro Ibayashi, MD; Kozo Iino, MD; Masatoshi Fujishima, MD

Background and Purpose  The aim of this study was to examine the levels of cerebral blood flow in relation to motor and cognitive functions in 300 chronic unilateral stroke patients (age, 64±12 years; mean±SD).

Methods  Cerebral blood flow was measured by the 133Xe inhalation method, adjusted for age, sex, and PCO2 level. Motor function was scored according to Brunnstrom hemiplegic staging and cognitive function according to the Hasegawa dementia rating scale tested in Japanese.

Results  Asymmetries of blood flow between affected and nonaffected hemispheres increased with lesion size and were highest in 11 embolic strokes (20±9%) and higher in 80 nonembolic cortical infarctions (11±11%) and 76 hemorrhages (9±7%) than in the group of 133 subcortical infarctions (2±6%) or 16 control subjects (1±2%). Severity of hemiparesis correlated with decreased cerebral blood flow in the affected hemisphere (P<.01) and increased hemispheric asymmetries of blood flow (P<.001). Cognitive impairments, after adjusting for age, correlated with decreased cerebral blood flow in the nonaffected hemisphere (P<.0001), left hemispheric lesions (P<.0005), and embolic stroke (P<.005) but not with asymmetries of blood flow. Among 67 patients having bilateral reductions of cerebral blood flow, 25 patients with left hemispheric lesions showed more severe cognitive impairments than among 42 patients with right hemispheric lesions (P<.05).

Conclusions  We confirmed that severity of hemiparesis correlated with the degree of asymmetries of cerebral blood flow, reflecting the extent and location of the lesions. Bilateral reductions of cerebral blood flow in patients with left hemispheric lesions may in part contribute to cognitive impairments, indicating reductions of global neuronal activities in the contralateral hemisphere or diffuse cerebrovascular changes. Further studies of cerebral metabolism and follow-up of cerebral circulation are required to reveal the pathophysiology and clinical consequences. (Stroke. 1994;25:309-317.)

Key Words  • cerebral blood flow  • hemiplegia  • xenon cognition

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Brain dysfunction after stroke closely relates to the site and extension of lesions and thus correlates with the degree of the reduction of cerebral blood flow (CBF).1-2 Reductions in intellectual functions may be associated with decreases in global neuronal activity caused by cortical or subcortical vascular lesions or both. Cognitive dysfunction correlates with diffuse CBF reductions,3-12 which usually is bilateral.10-12

The aim of this study was to examine levels of decreased CBF in relation to motor and cognitive functions in chronic stroke patients. Asymmetry of CBF between affected and nonaffected hemispheres may be a useful index for severity of the stroke,13-14 but bilateral CBF reductions are sometimes observed in patients with unilateral lesions.6-15-18 Therefore, the mental and neurological status was compared among the patients with bilateral, unilateral, and minimal CBF reductions. We also examined levels of CBF and brain functions associated with the location, size, and type of vascular lesions.

Subjects and Methods

From 1983 to 1988, CBF was examined in 541 consecutive patients in the Stroke Care Unit and Rehabilitation Center. Among them, 300 chronic stroke patients (183 men and 117 women; age, 64±12 years; range, 16 to 89 years) were selected for the present study. Inclusion criteria were patients with (1) completed stroke, (2) no previous or recurrent stroke, (3) unilateral supratentorial lesion (infarction or hemorrhage) confirmed by clinical examinations and brain computed tomography (CT) performed within 2 weeks after the stroke, (4) stable neurological and motor deficit for 1 month after onset of stroke, and (5) minimal hearing or visual deficits. Aphasic and left-handed patients were carefully excluded. Sixteen age-matched cases without stroke served as control subjects.

By CT criteria, 224 patients had cerebral infarctions and 76 had hemorrhages. One hundred seventy-eight patients had right hemispheric lesions and 122 had left lesions. Patients were classified into two subgroups: 91 with cortical lesions (17 anterior, 66 middle, and 8 posterior cerebral artery territory) and 209 with subcortical lesions (161 basal ganglia or white matter and 48 thalamus). Among 91 cortical infarctions, 11 were embolic and the other 80 were nonembolic. All embo-
lisms were cardiogenic. Among 80 nonembolic cortical infarctions, 71 were thrombotic and 9 were undetermined. Embolic stroke was not observed among subcortical infarctions. There were 76 patients with lacunae among 133 patients with subcortical infarctions. All hemorrhages were located in subcortical regions. Control subjects had no brain lesions by CT studies. Follow-up studies of CT were performed at the measurements of CBF to confirm that edema or hematoma had disappeared and that there was no recurrence of stroke.

The size of the hematoma was estimated as an oval shape by $[3.14 \times \text{length/2} \times \text{width/2}]$ of the hyperdense lesion in the slice showing the maximum area at the acute stage. The size of the infarcted lesion was estimated as an oval or a rectangle by multiplying the maximum length times width of the hypodense lesion in the slice showing the largest area at the chronic stage.

Regional CBF was measured by the $^{133}$Xe inhalation technique using a 22-probe (11 over each hemisphere) Novo-Cerebrograph with the patient in the resting condition with eyes closed, as described previously.\(^{19,20}\) The $^{133}$Xe gas mixture with air (3 mCi/L) was administered by means of a close-fitting face mask for 1 minute, and $^{133}$Xe clearance curves were examined for 10 minutes. The clearance curves were subjected to two-compartment analysis and the initial slope was used, since this is one of the most reliable flow parameters, relatively unaffected by compartmental instability (slippage) that may occur in the two-compartment analysis.\(^{21,22}\) The values from each detector were calculated and averaged to determine mean hemispheric CBF. Levels of blood pressure, expired end-tidal PCO$_2$ (Peco$^2$), hematocrit, and hemoglobin concentrations were simultaneously recorded. All CBF values were corrected to the Peco$^2$ level of 36.5 mm Hg, according to Maximilian et al.\(^{23}\) CBF=$-0.75 \times (\text{Peco}_2 - 36.5)$

Mean Peco$^2$ (±SD) for the entire sample was 34.6±3.7. Decrease in CBF was counted as significant when the values were under −2 SD from those of control subjects (≤35.1 milliliters per 100 grams per minute for the affected hemisphere and ≤34.8 milliliters per 100 grams per minute for the nonaffected hemisphere). The differences in CBF in affected and nonaffected hemispheres were expressed as percent asymmetries according to Mosmans et al.\(^{14}\)

% Asymmetry=$\frac{\text{CBF in nonaffected hemisphere} - \text{CBF in affected hemisphere}}{\text{mean CBF of both hemispheres}} \times 100$

All CBF measurements were made at least 1 month after stroke. The CBF measurements were made at 192 ± 300 days (median, 64) after the onset of stroke. Raw scores for CBF decreased with advancing age in the affected (−0.19 milliliters per 100 grams per minute per year, $P<.001$) and nonaffected hemispheres (−0.24 milliliters per 100 grams per minute per year, $P<.001$) among patients and in both hemispheres (−0.58 milliliters per 100 grams per minute per year, $P<.01$) among control subjects. After adjusting all to age 63, average CBF was lower in men than in women in the affected (−2.60 milliliters per 100 grams per minute, $P<.005$) and nonaffected hemispheres (−3.08 milliliters per 100 grams per minute, $P<.001$) among patients and in the left (−5.93 milliliters per 100 grams per minute, $P<.005$) and right hemispheres (−6.55 milliliters per 100 grams per minute, $P<.05$) for control subjects. Therefore, CBF was adjusted for age and sex according to the following equations:

**Male patients:**
- Affected hemisphere, CBF=$+0.19 \times (\text{age} - 63)$
- Nonaffected hemisphere, CBF=$+0.24 \times (\text{age} - 63)$

**Female patients:**
- Affected hemisphere, CBF=$+0.19 \times (\text{age} - 63) - 2.60$
- Nonaffected hemisphere, CBF=$+0.24 \times (\text{age} - 63) - 3.08$

Levels of hematocrit did not significantly correlate with CBF values.

Rehabilitation was performed for 14 to 341 days (138±70; median, 122) in our clinic. On the day of CBF measurement, motor function of each patient was evaluated using scores for Brunnstrom motor recovery scales.\(^{24}\) The movements of fingers, arms, and legs were classified into six scores; 6 points for normal to 1 for no voluntary movements. There were no significant correlations between age and scores for Brunnstrom stage.

We also evaluated the intellectual status on the day of CBF measurement with the use of the Hasegawa dementia rating scale (HDS).\(^{25}\) This dementia rating scale, which is very similar to the Mini-Mental State Examination, is a simple and reliable method and has been widely used in Japan to estimate cognitive impairments. This scale consists of five items to examine orientation, general information, calculation, memory, and memory recall. The full score is 32.5 points and the lowest is 0. Normal scores on HDS are ≥31; mild abnormality, 22 to 30.5; moderate, 10.5 to 21.5; and severe, ≤10 points. One hundred forty-seven patients (49%) showed normal scores on HDS (≥31). One hundred seven patients (36%) had scores of 22 to 30.5, 35 patients (12%) had scores of 11.5 to 21.5, and 11 patients (4%) had scores ≤10. Cognitive functional scores decreased with aging (−0.174 points per year). Therefore, scores for HDS in stroke patients were adjusted for age according to the following equation:

HDS+0.174×(age−63)

All data are expressed as mean±SD. Values of CBF between affected and nonaffected hemispheres were compared by paired t tests. Values of CBF, asymmetries, and functional scores between selected paired groups (patients versus control subjects, men versus women, or left versus right hemispheric lesions) were analyzed by unpaired t test or nonparametric Mann-Whitney U test. Values of CBF, asymmetries, and functional scores were compared among five groups; embolic cortical infarctions, nonembolic cortical infarctions, subcortical infarctions, cerebral hemorrhages, and control subjects were compared by analysis of variance (ANOVA) or nonparametric Kruskal-Wallis ANOVA and Scheffé's test. Values of CBF, asymmetries, and functional scores were compared among three groups for CBF characteristics (bilateral, unilateral, and minimal reductions) by ANOVA or nonparametric Kruskal-Wallis ANOVA and Scheffé's test. Patients with or without risk factors were compared by χ² tests. Correlation between CBF values and functional scores was analyzed using simple or multiple regression analysis. Pearson's correlation coefficients were used for the calculation of correlations. All probability values were based on two-sided tests. Differences were considered significant at $P<.05$.

**Results**

The characteristics of 300 patients and 16 control subjects are depicted in Table 1. Patients with cerebral hemorrhage were 7 to 8 years younger than nonembolic cortical and subcortical infarction groups ($P<.01$). Hematocrit was lower in stroke patients than in control subjects ($P<.05$). Hypertension was less frequent in the group with embolic infarctions (27%) than in patients with subcortical infarctions (73%, $P<.05$, Table 1). The size of the lesion was largest in embolic cortical infarctions (26±15 cm²), larger in nonembolic cortical infarctions (19±8 cm²) than...
that in hemorrhages (12 ±5 cm²), and smallest in subcortical infarctions (3 ±2 cm², Table 1).

**Profile of Cerebral Blood Flow**

After adjusting to 63-year-old men, average CBF was lower in the groups with cortical infarctions and hemorrhages compared with control subjects or the group with subcortical infarctions in the affected hemisphere (P<.01) and compared with control subjects in the nonaffected hemisphere (P<.05, Table 1). Values of CBF in the affected hemisphere were lower than those in the nonaffected hemisphere in stroke patients (P<.005). The patient group with embolism had the highest CBF asymmetries (20 ±9%), and the groups with bilateral and unilateral CBF reductions (7% and 42%, respectively), but there was no difference in asymmetries between patients with right (7 ±10%) and left lesions (6 ±8%). Risk factors, stroke type, and size and location of lesions were similar between the two groups.

Reductions of CBF in both hemispheres were observed in 67 patients (22.3%), and reductions in one hemisphere were observed in 52 patients (17.3%, Table 2). One hundred eighty-one patients (60.3%) showed minimal CBF reductions in both hemispheres. The frequencies of risk factors were similar between patients with bilateral and unilateral CBF reductions. Hypertension was less frequent among patients with bilateral CBF reductions (54%) compared with minimal reductions (73%), but 5 embolic patients showing bilateral hemorrhages by ANOVA and Scheffe’s test; **P<.05 for association with embolic cortical infarction by χ² test.

Table 1. Characteristics of 300 Patients and 16 Control Subjects

<table>
<thead>
<tr>
<th></th>
<th>Cortical Infarction</th>
<th>Subcortical Infarction</th>
<th>Hemorrhage</th>
<th>Stroke Patients (Total)</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Embolic n=11</td>
<td>Nonembolic n=80</td>
<td>n=133</td>
<td>n=78</td>
<td>n=16</td>
</tr>
<tr>
<td>Age, y</td>
<td>64 ±13</td>
<td>66 ±12*</td>
<td>65 ±10#</td>
<td>58 ±12</td>
<td>64±12</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>126±20</td>
<td>139±20</td>
<td>139±22</td>
<td>138±20</td>
<td>138±21</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>79±11</td>
<td>81±14</td>
<td>82±13</td>
<td>85±12</td>
<td>82±13</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>39±4</td>
<td>40:6</td>
<td>39±5</td>
<td>40±5</td>
<td>39±5</td>
</tr>
<tr>
<td>Size of lesion, cm²</td>
<td>26±15*</td>
<td>19±6*</td>
<td>3±2</td>
<td>12±5*</td>
<td>10±9</td>
</tr>
<tr>
<td>Cerebral blood flow (ISI), mL/100 g per min</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affected hemisphere</td>
<td>30±8*</td>
<td>35±8*</td>
<td>40±7</td>
<td>36±6*</td>
<td>37±8*</td>
</tr>
<tr>
<td>Nonaffected hemisphere</td>
<td>36±8*</td>
<td>38±7*</td>
<td>41±6</td>
<td>39±6*</td>
<td>39±6*</td>
</tr>
<tr>
<td>Hemispheric asymmetry, %</td>
<td>20±9*</td>
<td>11±11*</td>
<td>2±6</td>
<td>9±7*</td>
<td>7±9*</td>
</tr>
</tbody>
</table>

Scores for Brunnstrom stage (median)

- **Finger**: 2.4±1.7 (2)* 4.1±1.9 (5)* 4.7±1.5 (6) 4.0±1.7 (4.5)* 4.3±1.8 (5)* 6.0±0.0 (6)
- **Arm**: 2.9±1.9 (2)* 4.3±1.6 (5)* 4.8±1.4 (5) 4.1±1.4 (4)* 4.4±1.5 (5)* 6.0±0.0 (6)
- **Leg**: 3.3±1.8 (3)* 4.6±1.3 (5)* 5.0±1.5 (5) 4.5±1.2 (5)* 4.7±1.3 (5)* 6.0±0.0 (6)

Hasegawa dementia rating scale

- 19.9±8.0* 27.1±6.5 28.7±6.2 27.8±5.3 27.7±6.3* 31.1±0.9

Risk factors, No. of cases

- Hypertension**: 3 (27%) 45 (56%) 97 (73%) 55 (72%) 200 (67%) 11 (69%)
- Diabetes mellitus 4 (36%) 24 (30%) 53 (40%) 15 (20%) 96 (32%) 4 (25%)
- Hypercholesterolemia 3 (27%) 17 (21%) 29 (22%) 15 (20%) 64 (21%) 1 (8%)
- Atrial fibrillation**: 5 (45%) 6 (8%) 3 (2%) 1 (1%) 15 (5%) 1 (6%)
- Smoking 3 (27%) 40 (50%) 59 (44%) 23 (30%) 125 (42%) 4 (25%)
### TABLE 2. Reductions in Cerebral Blood Flow Within Bilateral or Unilateral Hemisphere in 300 Chronic Stroke Patients

<table>
<thead>
<tr>
<th>Hemispheric Cerebral Blood Flow</th>
<th>Bilateral Reduction n=67</th>
<th>Unilateral Reduction n=52</th>
<th>Minimal Reduction n=181</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>64±12</td>
<td>62±10</td>
<td>64±12</td>
</tr>
<tr>
<td>Male: female</td>
<td>42:25</td>
<td>34:18</td>
<td>107:74</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>135±21</td>
<td>134±20</td>
<td>141±21</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>82±13</td>
<td>81±14</td>
<td>83±13</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>40±5</td>
<td>39±4</td>
<td>39±5</td>
</tr>
<tr>
<td>Size of lesion, cm²</td>
<td>13±11†</td>
<td>15±10†</td>
<td>8±8</td>
</tr>
<tr>
<td>Cerebral blood flow (initial slope Index)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affected hemisphere, ml/100 g per min</td>
<td>28±4†§</td>
<td>32±2†</td>
<td>42±5</td>
</tr>
<tr>
<td>Nonaffected hemisphere, ml/100 g per min</td>
<td>31±3†§</td>
<td>38±2†</td>
<td>43±5</td>
</tr>
<tr>
<td>Hemispheric asymmetry, %</td>
<td>11±11††</td>
<td>16±8†</td>
<td>3±5</td>
</tr>
<tr>
<td>Brunnstrom stage (median)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Finger</td>
<td>3.5±1.9 (3)†</td>
<td>3.4±1.8 (3)†</td>
<td>4.8±1.5 (5)</td>
</tr>
<tr>
<td>Arm</td>
<td>3.7±1.6 (3)†</td>
<td>3.7±1.6 (3)†</td>
<td>4.9±1.3 (5)</td>
</tr>
<tr>
<td>Leg</td>
<td>4.0±1.3 (4)†</td>
<td>4.2±1.4 (4)†</td>
<td>5.1±1.0 (5)</td>
</tr>
<tr>
<td>Hasegawa dementia rating scale</td>
<td>25±8†</td>
<td>27±8*</td>
<td>29±5</td>
</tr>
</tbody>
</table>

Values are mean±SD. *P<.05, †P<.001 vs patients with minimal reduction by analysis of variance (ANOVA) or Kruskal-Wallis ANOVA and Scheffe's test; †P<.005, §P<.001 vs unilateral reduction by ANOVA and Scheffe's test.

46%, respectively). Atrial fibrillation (12%), hemorrhagic stroke (38%), and right-sided lesions (77%) were also more frequent in patients with unilateral reduction than in those with minimal reductions (3%, 21%, and 53%, respectively). Average CBF in both hemispheres was lower in patients showing bilateral CBF reductions than in those having unilateral reductions (Table 2). Asymmetries of CBF were highest in patients having unilateral hemispheric reductions of CBF (16±8%), and patients having bilateral CBF reductions (11±11%) showed higher asymmetries than those having minimal CBF reductions (3±5%, Table 2).

**Motor Function**

Eighty-two patients (27%) achieved complete recovery of motor function within 9 months after the onset. Average scores for finger movement were slightly but significantly lower (4.3±1.8) than those of arms (4.4±1.5, P<.05), and scores for leg motion were highest among the stroke patients (4.7±1.3, P<.001). Scores for Brunnstrom stage for fingers (2.9±1.7), arms (2.9±1.9), and legs (3.3±1.8) were lowest among embolic patients. Patients with hemorrhages or nonembolic cortical infarctions showed lower motor scores than control subjects (Table 1). The size of the lesion was significantly correlated with scores for motor function by simple regression analysis (r=-.189, P<.005). Cognitive scores in patients with left hemispheric lesions (22±7) were lower than in those with right lesions (29±6, P=.01). Cognitive scores were lower in patients with bilateral or unilateral CBF reductions than in those with minimal reductions (P<.001 and P<.05, respectively; Table 2). The difference did not reach statistical significance between scores in patients with bilateral and unilateral CBF reductions (Table 2).
Cognitive scores correlated with CBF in affected and nonaffected hemispheres (P<.001, Fig 2) but not with CBF asymmetries. Fig 3 shows the scores on HDS among six subgroups according to the side of the lesions and bilateral, unilateral, or minimal hemispheric CBF reductions. Of 122 patients with a left lesion, 25 (20%) showed bilateral CBF reduction, 12 (10%) showed unilateral reduction, and 85 (70%) showed minimal reduction. Of 178 patients with a right lesion, 42 (24%) showed bilateral CBF reduction, 40 (22%) showed unilateral reduction, and 96 (54%) showed minimal reduction. Patients with left lesions having bilateral CBF reduction showed the lowest HDS scores, and their scores were significantly lower than in 42 patients with right lesions having bilateral CBF reduction (P<.001) and in 85 patients with left lesions having minimal CBF reductions (P<.05, Fig 3). Among the patients with bilateral CBF reduction, CBF in affected and nonaffected hemispheres or CBF asymmetries were similar between right (28±5 and 31±3 milliliters per 100 grams per minute, respectively, or 12±12%) and left hemispheric lesions (29±4 and 32±3 milliliters per 100 grams per minute, respectively, or 9±9%).

By multiple regression analysis, cognitive impairments significantly correlated with (1) decreased CBF in the nonaffected hemisphere (P<.0001), (2) left hemispheric lesions (P<.0005), and (3) embolic stroke (P<.005, Table 3).

**Discussion**

In this study, CBF data were obtained after 1 month or more from the onset of stroke to avoid compliance difficulties frequently encountered during the acute stage and to avoid the confounds of brain edema or intracranial hypertension. In our study, brain edema was considered to have resolved within the first 4 weeks according to the findings of follow-up CT scans; thus,

**Table 3. Standardized Multiple Regression Coefficients for Brunnstrom Stage and Hasegawa Dementia Rating Scale Regressed on CBF in Affected and Nonaffected Hemispheres, Hemispheric CBF Asymmetries, Stroke Type, Side, Location and Size of Lesions, Sex, and Systolic Blood Pressure in 300 Chronic Stroke Patients**

<table>
<thead>
<tr>
<th>Rank</th>
<th>CBF in affected hemisphere</th>
<th>Systolic blood pressure</th>
<th>Embolic stroke</th>
<th>Lesion size</th>
<th>Hasegawa dementia rating scale</th>
<th>Male sex</th>
<th>Lesion size (left hemisphere)</th>
<th>Lesion location (cortex)</th>
<th>Hemorrhagic stroke</th>
<th>Male sex</th>
<th>Lesion location (cortex)</th>
<th>Hemispheric CBF asymmetry</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.420</td>
<td>-0.168</td>
<td>-0.089</td>
<td>0.303</td>
<td>0.057</td>
<td>-0.037</td>
<td>0.025</td>
<td>0.004</td>
<td>-0.042</td>
<td>-0.022</td>
<td>-0.006</td>
<td>2.513</td>
</tr>
<tr>
<td>2</td>
<td>0.176</td>
<td>0.140</td>
<td>0.080</td>
<td>0.103</td>
<td>-0.084</td>
<td>-0.057</td>
<td>-0.006</td>
<td>-0.004</td>
<td>0.034</td>
<td>0.007</td>
<td>-0.070</td>
<td>19.893</td>
</tr>
</tbody>
</table>

CBF indicates cerebral blood flow.

*Statistically significant.
there were minimal (if any) effects of edema on the results.²⁰ Assessments of brain functions were likewise completed after maximum recovery from stroke. The first assessment of HDS made at the beginning of rehabilitation was not used because it is not always the best score for each patient, and recovery had already occurred in some cases. Moreover, many factors associated with therapy influence functional assessment during the acute and subacute stages. During the recovery period, CBF remains virtually unchanged despite improvement of clinical symptoms.²⁶²⁷ Little attention has been paid, however, to correlation between clinical status and CBF after full recovery from a stroke insult.

Absolute values for CBF vary for each individual according to the level of PCO₂,²³ age,¹⁹²⁸ and sex.²⁹ Hematocrit did not significantly correlate with CBF in our patients, probably because of the relatively small range of variation (5% of SD). We corrected CBF values for the level of PCO₂, age, and sex in order to examine direct relations between brain functions and CBF. Even after these corrections, absolute CBF values varied; therefore, comparison between affected and nonaffected hemispheric CBF, termed hemispheric CBF asymmetry, is a more reasonable and reliable CBF assessment after stroke.

Data of CBF obtained by ¹³³Xe inhalation should be interpreted with caution because of several technical limitations: (1) there are several drawbacks that are inherent in the two-dimensional CBF methods (“lookthrough” phenomenon³⁰ and Compton scatter²¹⁻³¹), (2) asymmetry of CBF is influenced by cross-talk,³² (3) no attention was paid to focal CBF abnormalities because of bias toward cortical lesions and limitation of sensitivity,³³⁻³⁴ (4) the inhalation method has problems of airway artifacts or pulmonary dysfunction,³⁵ (5) CBF during rest is influenced by the patient’s mental state, such as wakefulness or anxiety, and (6) CBF, providing information only about hemodynamic aspects of circulation, may not always reflect cerebral metabolism even after full recovery from stroke.

Despite the severe limitations with much less advanced equipment, our findings may suggest a different...
tendency of CBF behavior in the same group of patients. The major findings in the present study may be summarized as follows: (1) the severity of hemiparesis correlated directly with the severity of decreased CBF in the affected hemisphere and with increased asymmetries of CBF between affected and unaffected hemispheres, and (2) declines in cognitive function were closely related to decreased CBF in the nonaffected hemisphere (or bilateral CBF reductions), left hemispheric lesions, and embolic strokes.

In chronic stroke patients, the degree of CBF reductions in the affected hemisphere (or CBF asymmetries) correlated with the severity of the stroke and the extent of the lesions. As previously reported in patients with chronic putaminal hemorrhage, CBF reductions in the affected hemisphere correlated with the maximum hematoma volume in the acute stages, which may directly reflect the extent of the lesion. In patients with deep-seated lesions, CBF reductions ipsilateral to the lesion may be predominantly remote effects called transneuronal depression. Asymmetries of CBF were greater in patients with cortical infarctions and hemorrhages than in those with subcortical infarctions. The larger extent of lesions in the cortex or subcortex may be reflected by the greater asymmetries, as shown in our data.

Bilateral CBF reductions were observed in 22% of all the patients, but the mechanisms are not fully known. Five possible explanations were considered: (1) transhemispheric diaschisis, (2) systemic circulatory disturbances, (3) underlying cerebral arterial changes associated with risk factors, (4) interhemispheric steal, and (5) decrease in global neuronal activities after stroke. First, a number of studies of CBF and metabolism have emphasized the evidence of transhemispheric diaschisis. Second, there was no heart failure, orthostatic hypotension, or other severe systemic circulatory disturbances present in our patients. Third, hypertension and other risk factors such as smoking and hyperlipidemia may play an important part in diffuse reductions of CBF. From our data, however, this is an unlikely explanation because the frequency and presence of such risk factors were similar between patients with bilateral and unilateral CBF reductions. Therefore, incidence of cerebrovascular changes associated with risk factors may be similar between two groups except for the embolic patients. It is not known whether CBF was already reduced before the stroke in patients showing bilateral CBF reductions; however, after the stroke, decreased CBF in the contra-lateral hemisphere appeared to correlate with global decreases in cognitive function. We assume that among patients suffering from declines in physical, mental, daily living, and social activities after stroke, global neuronal activities become decreased and CBF also may decrease in the contralateral hemisphere, coupling with decreased metabolic demands. Unilateral lesions were determined by clinical examinations and brain CT findings; more strict criteria using magnetic resonance imaging, and cerebral angiography would be required to avoid the coexistence of asymptomatic cerebrovascular changes and to reveal the mechanism of bilateral CBF reductions.

Even during rehabilitation, 73% of our patients still suffered motor deficit after recovery from stroke. The severity of hemiparesis correlated well with the degree of decreased CBF in the affected hemisphere and increased CBF asymmetries. The present results are in accord with previous reports that higher asymmetries are associated with neurological disability scores and angiographic findings, which primarily reflect severity of brain damage. Declines in motor function mainly are due to neuronal damage of the motor pathways, including the motor cortex, internal capsule, and basal ganglia. A larger size of lesion is primarily responsible for more severe motor impairment. However, anatomic localization for motor functions based on CT findings are reported to be different for each patient. A decrease in cortical blood flow (including motor cortex) ipsilateral to the lesion that is due directly to the cortical lesion, indirectly to transneuronal depression of the ipsilateral cortex from a subcortical lesion, or due to ipsilateral cerebrovascular changes appears to be one possible explanation for severe motor impairment. We speculate that even in some cases with small-sized, deep lesions, decrease in cortical neuronal activities, which may be coupled with decreased CBF, on the same side of the lesion may be in part associated with more severe motor deficits, resulting in increased asymmetries of CBF. We confirmed that asymmetry of CBF may be useful for evaluating motor impairments even after full recovery from stroke.

Cognitive scores correlated well with CBF in both hemispheres. In contrast to motor function, individual side-to-side asymmetries may have little significance on cognitive function, mainly because of bilateral CBF reductions. Decrease in cortical blood flow contralateral to the lesion resulting in bilateral CBF reduction by decreased neuronal activities caused by transhemispheric diaschisis and declines in physical, mental, daily living, and social activities may partially contribute to severe cognitive impairment. Our study suggested that left hemispheric lesions among patients having bilateral CBF reductions are important contributors to declines in cognitive functions despite higher global CBF than patients with right hemispheric lesions. It appears, therefore, that left hemispheric lesions are more responsible for cognitive impairments than those affecting the right hemisphere. Impaired accuracy of responses and slower response time to multiple-choice paradigms have been reported among patients with left hemispheric brain damage compared with right hemispheric damage. Robinson et al reported post-stroke depression to be associated with global intellectual impairments, especially with left anterior lesions. Thus, impaired processes for cognition, and possibly mood changes, may be responsible for global cognitive decline in patients with left hemispheric lesions.

Patients with embolic stroke that was correlated with cognitive impairment (Table 3) showed the largest size of lesion (Table 1). Although lesion size failed to be correlated with functional scores by multiple regression analysis, we cannot deny the primary importance of lesion size, which was closely correlated with individual functional impairment by simple regression analysis. We doubt that the lesion size is very important for functional outcome. In patients with multiple infarcts, intellectual impairment was correlated with infarct volume. The main reason for our failure may be that we could not detect the precise size of the irregular shape.
of lesion by two-dimensional analysis. More accurate morphological estimation of lesion volume by three-dimensional analysis would be required.

HDS scores correlated well with CBF reductions and with other intelligence tests, as previously reported. In chronic stroke patients with dementia, the mean values for CBF are reduced bilaterally, which is a characteristic difference from that of patients without dementia. Furthermore, CBF reductions in frontal and temporal cortex (bilaterally) and thalamus have been reported to correlate with severity of cognitive impairment in patients with multi-infarct dementia. The technique of $^{133}$Xe CBF measurement is greatly biased toward cortical lesions, and we cannot detect CBF in deep structures by this technical limitation. We have recently shown that CBF reductions in the deep white matter measured by positron emission tomography (PET) are associated with declines in oxygen metabolism in demented patients. Although the association of cognitive dysfunction and bilateral reduction in CBF may be complex and multifactorial, further examinations concerning cerebral metabolic changes by PET studies could reveal direct metabolic functional relations.

The brain is a complex organ having many structural and functional components that not only operate separately but also cooperate with each other through neuronal pathways to maintain integrated function. Clinical implications of these complex and multifactorial phenomena should be done carefully. We preliminarily assessed the relation between CBF and brain functions in 300 unilateral stroke patients after full recovery from stroke. Despite limitations on methods and interpretations, our findings may give information about different tendencies of CBF behavior associated with the functional impairments among the same group of patients. We confirmed that severity of hemiparesis correlates with the degree of CBF asymmetries between affected and nonaffected hemispheres and thus reflects the extent and location of the lesion in the affected hemisphere. In contrast, bilateral reductions in CBF resulting from a left hemisphere lesion contribute to declines of cognitive function. The precise mechanism of this phenomenon is not yet known. It would be interesting to further analyze the possible relations among the lesion size, cerebral metabolism, vascular changes, and brain-specific functions. Follow-up study of CBF may also be useful to interpret clinical consequences.

References

44. Meyer JS, Rogers RL, Mortel KF, Judd BW. Hyperlipidemia is a risk factor for decreased cerebral perfusion in stroke. Arch Neurol. 1987;44:418-422.
Relation of cerebral blood flow to motor and cognitive functions in chronic stroke patients.
S Mori, S Sadoshima, S Ibayashi, K Lino and M Fujishima

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