Regional Cerebral Blood Flow Correlates of Aphasia Outcome in Cerebral Hemorrhage and Cerebral Infarction

Ken Nagata, M.D.*, Kazuta Yunoki, M.D.,† Sumie Kabe,‡ Atsuko Suzuki,‡ and Goro Araki, M.D.§

SUMMARY The relationship between recovery from aphasia and regional cerebral blood flow (CBF) was compared in 87 patients, 44 with cerebral hemorrhage and 43 with non-embolic cerebral infarction. CBF values correlated poorly with aphasia outcome in patients with cerebral hemorrhage whereas a tight correlation was demonstrated in patients with non-embolic cerebral infarction. A marked variability of CBF values in the acute and subacute stage might account for the poor correlation between CBF and aphasia outcome in patients with cerebral hemorrhage. On the other hand, a sharp discrimination was achieved between those with a good recovery from aphasia and those with a poor recovery by the dimensions of the hematoma on CT. In non-embolic cerebral infarction, a relative frontal ischemia was associated with motor aphasia while a relative temporal ischemia was associated with sensory aphasia. This dichotomy was not demonstrated in the regional CBF values in patients with cerebral hemorrhage.

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CEREBROVASCULAR DISEASE is known to be the leading cause of aphasia in adult patients. However, in many of the previous reports linking aphasias to cerebrovascular disease, there has been a tendency toward grouping different pathologic etiologies under the simple term "stroke." We previously reported† that cerebral blood flow (CBF) and the evolution of aphasia differed between embolic and non-embolic infarcts, supporting the necessity for identifying a specific etiologic basis for correlation.

In cerebral infarction, the anatomical substrates of aphasia have been studied with radionuclide scanning‡ and computerized tomography (CT). The studies showed that the aphasia outcome in these patients depends mainly upon the magnitude of the ischemic damage. Localization of the ischemic lesions indicated by these methods§ was consistent with the classically defined types of aphasia which were based on autopsy correlations. Regional CBF studies** also suggested a correlation between the clinical manifestations of aphasia and CBF levels in patients with cerebral infarction. Cerebral hemorrhage has been included in a number of reports correlating symptomatology with clinical outcome, pathologic findings, and neuroradiological findings. However, there has not been a systematic study of aphasia and its underlying pathophysiology as it relates to ischemic cerebrovascular disease. In this study, we have examined the relationship between aphasia and CBF in patients with intracerebral hemorrhage and those with non-embolic cerebral infarction.

Patients and Methods

The present study was based on 87 patients with left hemispheric cerebrovascular diseases: 44 patients with hypertensive intracerebral (putaminal) hemorrhage of which 24 patients were found to have aphasia and 43 patients with non-embolic cerebral infarction in the territory of the left middle cerebral artery, all of whom presented with aphasia. Patients who had a previous episode, and/or those who had a right hemisphere lesion or lesion in the verteobasilar arterial territory, in addition to the left hemisphere lesion, were excluded from the study. Diagnosis of non-embolic infarction was based on the findings on repeat CT and angiography. Those who had a marked mass effect of hemorrhagic infarction on CT, and those who showed a migration of the emboli or re-opening of the occluded vessels on repeat angiography were defined as having a probable embolic etiology and were excluded from the study. All patients were right-handed. Their mean age was 58.5 (38–83) years. No surgical treatment was carried out in these patients.

The course of aphasic syndrome was evaluated in 20 of 43 aphasic patients with cerebral infarction and in 20 of 44 patients with cerebral hemorrhage. The initial assessment of aphasia was carried out between 2 to 4 weeks after onset and the final assessment was performed at least 3 months after onset when the recovery of aphasia had reached a plateau. The severity of the aphasia was evaluated according to the modified Hira-no's scale, which was based on the patients' abilities in 5 modalities of verbal communication: spontaneous speech, auditory comprehension, writing, reading and repetition. The patients were classified into 3 categories: mild, moderate or severe deficits. The degree of recovery was evaluated by comparing the scores of the initial assessment with the scores of the final assessments. Since all patients subjected to this evaluation were regarded as having severe deficits at the initial assessment, those who recovered to moderate or mild deficits were defined as having made a "good recovery," and those who showed no significant improvement were defined as having made a "poor recovery.

The clinical types of aphasia were compared with rCBF values in all 43 patients with aphasia due to
cerebral infarction and in 20 patients with aphasia due to cerebral hemorrhage. Based on the results of the Standard Language Test for Aphasics (SLTA), the Western Aphasia Battery and the Token Test which were carried out in the chronic stage, the patients were classified as exhibiting global aphasia, motor aphasia, sensory aphasia or amnestic aphasia.

The CT sections parallel to the orbitomeatal line were used for this study. The CT findings of cerebral hemorrhage were classified into one of three types: localized, advanced with destruction of the internal capsule, or advanced with ventricular rupture. The dimensions of the hematoma was measured in both longitudinal (anteroposterior) and transverse (right-left) axes on the section in which the area of the hematoma was largest.

Regional CBF studies by 133-Xe intra-arterial method were carried out in 63 patients who were subjected to the direct carotid angiography. The measurements were performed in a quiet room in which the patients were lying on bed in relaxed mental (resting) state. After direct carotid angiography, the tip of the catheter was placed in the left internal carotid artery, and 3 mCi of 133-Xe dissolved in isotonic saline was injected as a bolus. The clearance curve was recorded with 16-channel detector system according to the initial slope index (ISI) method. During the rCBF measurements, PaCO₂ was monitored in an arterial blood sample taken from the catheter in the left internal carotid artery; there was no significant difference in PaCO₂ levels among the patient groups. The mean value of all 16 probes over the left hemisphere was used as a left hemispheric mean flow (mCBF). The rCBF value labeled “F” was derived from the average of three probes over the left frontal lobe which included Broca’s area and the rCBF value labeled “T” was derived from the average of three probes over the left temporal lobe including Wernicke’s area (fig. 1). The spatial relationship between the placement of detectors and the anatomical structure of the brain was confirmed on the plain skull films in which the location of the detectors was marked by lead tips following the rCBF examination (fig. 1). With this rCBF measurement system the normal value for the mCBF was 63.2 ml/100 g/min with a standard deviation of 11.8 ml/100 g/min.

Results

Recovery of aphasia vs rCBF values. Twelve out of 20 patients with cerebral hemorrhage made a good recovery from aphasia, whereas 8 patients made a poor recovery. Figure 2 shows a relationship between the degree of recovery from aphasia and mCBF values in these patients. There was a marked variability of mCBF values in the acute to subacute stage of cerebral hemorrhage. No particular correlation was seen between mCBF values and recovery from aphasia in these patients. Figure 3 shows relationship of F and T values with recovery from aphasia, and no particular correlation was found for either the “good recovery” group or the “poor recovery” group.

In 20 patients with cerebral infarction, 9 patients made a good recovery from aphasia while the other 11 patients made a poor recovery. Although there was a gradual increase of mCBF values in the late stage (4 weeks postictal), the time course of mCBF was stabilized in the acute and subacute stage (fig. 4). There was a tendency for mCBF values to be higher in those patients who made a good recovery from aphasia than those who made a poor recovery. This tendency persisted for the F and T values (fig. 5).

Table 1 shows a statistical comparison between good and poor recovery for each of the 3 parameters designated for CBF averaging. Student’s t-test was employed in these analyses. In the patients with cerebral hemorrhage, the mCBF was 33.1 ± 9.7 ml/100 g/min (52.3% of the normal CBF value) in the good recovery group and was 31.8 ± 10.3 ml/100 g/min (48.9%) in the poor recovery group. The difference in
mCBF between the good recovery and poor recovery groups was not statistically significant. The same was observed for both F and T values between the two groups. In contrast, the patients with cerebral infarction who made a good recovery had significantly higher CBF values (mCBF, F and T) than those who made a poor recovery (p < 0.001).

Recovery from aphasia and CT findings in cerebral hemorrhage. Table 2 shows a relationship between the CT findings and aphasia outcome in 44 patients with cerebral hemorrhage. Of 18 patients who showed a localized hematoma on CT only 3 presented with aphasia, and 2 of the 3 made a good recovery. Of 23

<table>
<thead>
<tr>
<th>Good recovery</th>
<th>Poor recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral hemorrhage</td>
<td></td>
</tr>
<tr>
<td>Mean age</td>
<td>54.1 ± 12.9 ns</td>
</tr>
<tr>
<td>mCBF</td>
<td>33.1 ± 9.7</td>
</tr>
<tr>
<td>F</td>
<td>33.4 ± 9.0</td>
</tr>
<tr>
<td>T</td>
<td>35.0 ± 11.7</td>
</tr>
<tr>
<td>n = 12</td>
<td>n = 8</td>
</tr>
<tr>
<td>Cerebral infarction</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>58.7 ± 11.1 ns</td>
</tr>
<tr>
<td>mCBF</td>
<td>38.2 ± 8.5 *</td>
</tr>
<tr>
<td>F</td>
<td>38.3 ± 8.7 *</td>
</tr>
<tr>
<td>T</td>
<td>36.7 ± 8.8 *</td>
</tr>
<tr>
<td>n = 9</td>
<td>n = 11</td>
</tr>
</tbody>
</table>

*p 0.001.
patients presenting with an advanced hematoma with destruction of the internal capsule all had aphasia and 18 of the 23 made a poor recovery from aphasia. All patients with an advanced hematoma rupturing into the ventricle made a poor recovery. The aphasia outcome was associated with the degree of extension of the hematoma as shown on CT. Table 3 shows a comparison of aphasia outcome and dimensions of hematomas on CT. Both longitudinal and transverse diameters were largest in the patients making a poor recovery and they were smallest in the patients without aphasia. Discrimination between the 3 groups of patients could be made on the basis of the longitudinal dimension of the clot at the 0.001 confidence level. Discrimination could be made between the good and poor recovery groups on the basis of the transverse dimension of the clot but there was no significant difference between patients presenting without aphasia and patients making a good recovery from aphasia based on the transverse dimension of the intracerebral hematoma. Thus, the degree of recovery from aphasia due to cerebral hemorrhage inversely correlated with the dimension of hematoma on CT.

**Clinical types of aphasia and CBF values.** Table 4 shows a comparison of CBF values associated with different clinical types of aphasia. In the patients with cerebral hemorrhage, the T value was higher than the F value in global aphasia (p < 0.05). In motor aphasia, sensory aphasia and amnestic aphasia, the F and T values were close to each other. In the patients with cerebral infarction, on the other hand, the F value was significantly lower than the T value in motor aphasia (p < 0.01), while the T value was significantly lower than the F value in sensory aphasia (p < 0.001). No obvious difference was found between F and T values in global aphasia and amnestic aphasia.

### Discussion

The greatest improvement of aphasia is considered to occur in the first 6 months following onset, particularly in the first 3 months. The fate of aphasic patients is greatly influenced by the etiology of aphasia, its initial type, and severity, and by the patient's age. Speech therapy is not considered to be crucial for the recovery from aphasia. In the patients selected for this study, their age and the severity of aphasia at the initial assessment were matched among the patient groups. Then the course of the aphasia was observed in relation to the CBF values and CT findings for at least the first 3 months following stroke. The results of this study indicate a distinct difference in the correlation of CBF with an aphasia outcome between the patients with cerebral hemorrhage and those with cerebral infarction. In contrast to the poor correlation between CBF and an aphasia outcome in patients with cerebral hemorrhage, the patients with cerebral infarction showed a direct correlation between CBF values and the degree of recovery from aphasia.

Demeyrisse and co-workers found a poor correlation of rCBF values with the outcome of motor function and functional independence in patients with cerebral infarction. Their rCBF determinations were made using the 133-Xe inhalation method over a period of 15 to 90 days following the onset of disease. They also suggested that the clinical improvement was not accompanied by a progressive normalization of rCBF values. Conflicting somewhat with the above conclusions, our previous report showed a good correlation between CBF levels and degree of recovery from aphasia in the patients with non-embolic cerebral infarction although the number of the subjects was limited. Using the 133-Xe intra-arterial method, Heiss and associates reported that CBF values as measured between 1 to 8 weeks following their stroke correlated significantly with the clinical score and outcome including higher brain function and psycho-organic syndrome in 180 patients with cerebral infarction. Tagawa and associates studied 46 aphasic patients utilizing 133-Xe inhalation method. The mCBF values measured in the chronic stage correlated significantly with the severity of aphasia. The results of the present study were in accordance with these previous reports on cerebral infarction. The mCBF value in the patients with a good recovery was 60.4% of the normal flow value. This is approximately the critical flow level below which irreversible neurological deficits occurred in the previous

### Table 2

Classification of CT Findings and Aphasia Outcome in the Patients with Cerebral Hemorrhage

<table>
<thead>
<tr>
<th>CT findings</th>
<th>Patients with a good recovery</th>
<th>Patients with a poor recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients without aphasia n = 20</td>
<td>Patients without aphasia n = 12</td>
</tr>
<tr>
<td>Localized</td>
<td>15</td>
<td>2</td>
</tr>
<tr>
<td>Advanced with destruction of internal capsule</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Advanced with ventricular rupture</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

### Table 3

Comparison of Dimensions of Hematoma on CT and Aphasia Outcome in Patients with Cerebral Hemorrhage

<table>
<thead>
<tr>
<th></th>
<th>Patients without aphasia n = 20</th>
<th>Patients with a good recovery n = 12</th>
<th>Patients with a poor recovery n = 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>53.8 ± 13.6 ns</td>
<td>54.7 ± 9.3 ns</td>
<td>56.4 ± 8.4 years</td>
</tr>
<tr>
<td>Longitudinal diameter</td>
<td>25.9 ± 12.3 *</td>
<td>34.6 ± 9.6 *</td>
<td>52.4 ± 9.8 mm</td>
</tr>
<tr>
<td>Transverse diameter</td>
<td>17.5 ± 8.6 ns</td>
<td>19.8 ± 5.8 †</td>
<td>28.8 ± 7.6 mm</td>
</tr>
</tbody>
</table>

ns: statistically not significant, *p < 0.001, †p < 0.01.
The appearance of brain edema can be associated with the first 2 weeks following cerebral hemorrhage.31,32 Ery. Brain edema is felt to appear and to resolve during edema with a small hematoma and showed a good correlation between the recovery of CBF and clinical recovery. Eight of these patients presented with a small hematoma and showed a good correlation between the recovery of CBF and clinical recovery. Brain edema is felt to appear and to resolve during the first 2 weeks following cerebral hemorrhage.31,32 The appearance of brain edema can be associated with an increase in intracranial pressure (ICP). With the 133-Xe intra-arterial method, Tazawa and associates32 reported no significant relationship between ICP levels and the ipsilateral mCBF values in patients with cerebral hemorrhage, although the ipsilateral mCBF values were all reduced below the normal range. However, in relieving brain edema by intravenous administration of hypertonic solution (10% Glycerol), a significant increase of CBF was observed in the region surrounding the hematoma. They suggested that brain edema may be a significant factor in the alteration of CBF levels in cerebral hemorrhage. In the study by Ishii and associates,30 the reduction of the ipsilateral mCBF was greater in those with a mass effect on CT, but some patients still present reduced CBF values even after the decompression surgery. With regard to the relationship between the size of hematoma and CBF values, Tazawa and associates32 suggested a poor correlation between the maximum diameter of hematoma and the ipsilateral mCBF values. In contrast, Ishii and associates30 reported that the volume of hematoma calculated from the CT data correlated positively with the reduction of the ipsilateral mCBF values. Clearly, these disparate reports make it difficult to extract a certain relationship between the CBF levels and the effects of hematoma and its surrounding edema.

It is of interest that CBF was normal in one patient with cerebral hemorrhage even though he showed a poor recovery. This was considered to be due to a pathological increase of CBF in the acute stage of cerebral hemorrhage. With the 133-Xe intra-arterial method, Kawakami and associates33 reported that relative hyperemia was observed in 16 out of 44 patients with cerebral hemorrhage. In the study with positron emission tomography by Ackerman and associates,34 there was a relative increase in CBF and glucose metabolism in the intact cortical area adjacent to the hemorrhage while CBF and glucose metabolism were depressed in the clot and the surrounding edematous area. In the experimental studies of basal ganglionic hemorrhage, Ropper and Zervas35 substantiated the presence of a substance in the clot which may cause the appearance of brain edema.

### Table 4: Comparison of CBF Values According to the Clinical Types of Aphasia

<table>
<thead>
<tr>
<th>Clinical Type of Aphasia</th>
<th>Global aphasia</th>
<th>Motor aphasia</th>
<th>Sensory aphasia</th>
<th>Amnestic aphasia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cerebral hemorrhage</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mCBF</td>
<td>28.3 ± 8.6</td>
<td>32.6 ± 9.9</td>
<td>20.5 ± 7.8</td>
<td>36.0 ± 9.5</td>
</tr>
<tr>
<td>F</td>
<td>26.0 ± 7.9</td>
<td>31.7 ± 11.0</td>
<td>22.0 ± 8.5</td>
<td>36.0 ± 8.8</td>
</tr>
<tr>
<td>T</td>
<td>31.3 ± 8.6</td>
<td>31.1 ± 8.2</td>
<td>22.5 ± 10.6</td>
<td>38.3 ± 11.4</td>
</tr>
<tr>
<td>n = 3</td>
<td>n = 9</td>
<td>n = 2</td>
<td>n = 6</td>
<td></td>
</tr>
<tr>
<td><strong>Cerebral infarction</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mCBF</td>
<td>23.3 ± 7.0</td>
<td>35.8 ± 9.5</td>
<td>28.4 ± 7.7</td>
<td>34.0 ± 4.5</td>
</tr>
<tr>
<td>F</td>
<td>21.9 ± 7.3</td>
<td>33.9 ± 8.9</td>
<td>31.7 ± 9.3</td>
<td>33.0 ± 9.0</td>
</tr>
<tr>
<td>T</td>
<td>22.8 ± 7.9</td>
<td>37.7 ± 10.3</td>
<td>25.0 ± 7.3</td>
<td>32.8 ± 8.5</td>
</tr>
<tr>
<td>n = 12</td>
<td>n = 20</td>
<td>n = 7</td>
<td>n = 4</td>
<td></td>
</tr>
</tbody>
</table>

ns: statistically not significant, *p ≤ 0.05, †p ≤ 0.01, ‡p ≤ 0.001.
cortical hyperperfusion. Thus, multiple factors might be involved in the alteration of CBF levels in patients with cerebral hemorrhage.

The methodological limitation of the isotope clearance method should be taken into consideration in discussing these results. With the 254 channel rCBF measurements by the 133-Xe intra-arterial method, Olsen and associates reported that when there was severe infarct in which isotope was not perfused, the blood flow values over this area were massively influenced by the blood flow of the neighboring tissues. They pointed out that the blood flow levels in the infarcted areas determined by the 133-Xe intra-arterial method were not in accordance with the ischemic threshold of CBF based on experimental studies. Compton scatter and look-through phenomena may invalidate the results of the rCBF measurements done using a conventional stationary detector system. A similar situation could be considered for the patients with cerebral hemorrhage: if isotopes cannot enter the clot, the blood flow levels over the region of the hematoma will reflect the blood flow of the surrounding tissues. In addition, the uncertainty as to the partition coefficient in the damaged or edematous tissue was a difficulty with this method. These factors may modify the results of CBF measurements for that region. In our results, however, the poor correlation between CBF values and recovery from aphasia was seen not only in the regional values but also in the mCBF values in the patients with cerebral hemorrhage. Although regional values may be unreliable utilizing this method, the mCBF values more reliably reflect the hemispheric circulation. The difference in the relationship of mCBF values to outcome of aphasia between cerebral hemorrhage and cerebral infarction was thought to reflect the differences in the pathophysiology of the aphasia between cerebral hemorrhage and cerebral infarction.

The use of the rCBF measurements as a diagnostic tool for predicting the degree of recovery from aphasia has obvious limitations in patients with cerebral hemorrhage. In contrast, CT provides a reliable diagnostic framework for predicting prognosis of aphasia. A good prognosis can be expected in patients with a localized hematoma on CT, and the prognosis of aphasia will be poor in those with an advanced-type hematoma with ventricular rupture. Furthermore, the diameters, particularly the longitudinal (anterior-posterior) diameter, of hematoma appeared to show a clear inverse correlation with aphasic recovery. These results indicate that it is anteroposterior compression rather than cortical ischemia which is the mediating factor in causing aphasia in cerebral hemorrhage. This confirms traditional views that putaminal hemorrhages manifest themselves with a broad spectrum of clinical presentations depending on the size of the hematoma. In a clinicopathological comparison between left putaminal hemorrhage and left thalamic hemorrhage, Alexander and Lo Verme pointed out that aphasia from cerebral hemorrhage was caused by destruction of the white matter from compression by the hematoma and surrounding brain edema rather than by a direct diencephalic injury or cortical damage. In CT studies, destruction of the deep white matter surrounding the hematoma was thought to be the principle factor in causing aphasia in cerebral hemorrhage. Heir and associates also suggested a correlation between the size of the hematoma and the severity and outcome of higher cortical dysfunction in patients with cerebral hemorrhage. In addition, there are many CT studies describing a relationship between the size of hematoma and clinical recovery in patients with cerebral hemorrhage. Thus, the size of hematoma on CT appears to be closely associated with the clinical recovery of aphasia in patients with cerebral hemorrhage. The CT scan has proven indispensable in diagnosing cerebral hemorrhages in their acute stage. In addition we feel that the usefulness of CT scan is extended since the prognosis in patients with aphasia due to cerebral hemorrhage can be made based on clot dimension.

It has been confirmed and supported by CT and rCBF studies in patients with cerebral infarction that nonfuent aphasia is caused by lesions anterior to the Rolandic fissure, while fluent aphasia is caused by lesions posterior to the fissure. In our present study, this dictum was also statistically supported in the patients with cerebral infarction. On the other hand, the association between the pre- and postrolandic lesions and fluent and nonfluent aphasia respectively was not demonstrated in the patients with cerebral hemorrhage. The methodological limitation of two-dimensional rCBF measurements using 133-Xe may have contributed significantly to the lack of correlation between rCBF and the types of aphasia in the patients with hemorrhage. Tomographic investigation by positron emission tomography or single photon emission tomography will circumvent the disadvantages of the two-dimensional rCBF measurements and make it possible to compare local CBF and metabolism between cerebral hemorrhage and cerebral infarction.

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