Cerebral Blood Flow in Subcortical Global Aphasia
Perisylvian Cortical Hypoperfusion as a Crucial Role

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Background and Purpose  Global aphasia after subcortical stroke is very rare, and its pathophysiology remains unsolved. To clarify the mechanism underlying subcortical global aphasia, we investigated lesion sites and cerebral blood flow in patients with subcortical global aphasia and nonaphasic patients with subcortical stroke.

Methods  We examined four patients with global aphasia and four nonaphasic patients. Language testing was performed more than 4 weeks after the onset. Measurement of cerebral blood flow was done between 35 and 75 days after stroke by using single-photon emission computed tomography (SPECT) with N-isopropyl-\(^{123}\)iodoamphetamine as a tracer and three-dimensional surface display generated from SPECT.

Results  All aphasic patients had subcortical lesions in the putamen, posterior internal capsule, temporal isthmus, and periventricular white matter in the left hemisphere. No cortical lesions were found on either magnetic resonance imaging or computed tomographic scanning. The nonaphasic patients had smaller periventricular white matter lesions and no temporal isthmus lesions. All aphasic patients showed cortical hypoperfusion mainly in the perisylvian areas, including Broca's and Wernicke's areas. In contrast, cortical cerebral blood flow of the nonaphasic patients was decreased in smaller areas and spared the perisylvian language areas.

Conclusions  These results suggest that cortical hypoperfusion in the perisylvian language areas, presumably due to undercutting of the white matter, is crucial for the development of subcortical global aphasia. (Stroke. 1994;25:1495-1499.)

Key Words  • aphasia • cerebral blood flow • diaschisis • cerebrovascular disorders • language

Although the incidence of global aphasia is relatively high in aphasic patients with cerebrovascular diseases, its pathophysiology has not yet fully been clarified. In patients with global aphasia all of the major language capacities are severely disturbed, but considerable variations exist in the clinical features and course of the syndrome. Some patients show good recovery from global aphasia, while others fail to improve for long periods. Most patients with global aphasia show changes to another aphasic syndrome, but some patients show persistent loss of communicative abilities. These facts demonstrate the heterogeneity of the pathophysiology of global aphasia. Global aphasia is usually caused by large cortical lesions, including those in Broca's and Wernicke's areas. However, some authors have classified global aphasia as a nonlocalizing type of aphasia. Clinicoanatomic studies have shown that global aphasia can result from anterior cortical, posterior cortical, combined cortical, or subcortical damage. Some authors have designated global aphasia after subcortical stroke as subcortical global aphasia. In these studies clinicoanatomic correlations have been estimated using computed tomographic (CT) scanning, but the causal relation between subcortical lesions and global aphasia remains unsolved. We therefore believed it necessary to elucidate the functional damage to cortical and subcortical structures in subcortical global aphasia. Accordingly, we investigated cerebral blood flow of patients with global aphasia and without aphasia after subcortical stroke using single-photon emission computed tomography (SPECT) and N-isopropyl-\(^{123}\)iodoamphetamine (\([^{123}\text{I}]\text{IMP}\)) as a tracer. To visualize the cortical perfusion defects, a three-dimensional surface display was generated from \([^{123}\text{I}]\text{IMP}\) SPECT.

Subjects and Methods

Subjects  Eight right-handed patients with subcortical stroke participated in this study. The aphasic group (patients 1 to 4; 3 men and 1 woman, aged 58 to 81 years) included 2 patients with infarction (patients 1 and 2) and 2 patients with hemorrhage (patients 3 and 4). All aphasic patients presented with persistent disturbance of major language abilities, remaining in the state of global aphasia. As a comparison with the aphasic patients, we examined 4 nonaphasic patients with relatively large subcortical lesions (patients 5 to 8; 3 men and 1 woman, aged 60 to 81 years). We selected these patients because the other patients with larger subcortical lesions tended to show impairments of language abilities in various degrees. The nonaphasic group included 3 patients with infarction (patients 5, 6, and 7) and 1 patient with hemorrhage (patient 8). Three of the nonaphasic patients showed normal speech, but 1 patient (patient 7) had mild dysarthria of the pseudobulbar type. All 8 patients had right hemiparesis. To confirm the extent of lesions, magnetic resonance imaging (MRI) or CT scanning was performed between 18 and 60 days after stroke. Seven patients underwent both MRI and CT scanning; 1 patient (patient 4) underwent CT scanning only.
Cerebral Blood Flow Examination

To assess cerebral blood flow in the two groups, [123I]IMP SPECT was performed between 35 and 75 days after stroke when global aphasia was still present in the aphasic group. Early and delayed images of SPECT were conducted 30 minutes and 5 hours after administration of [123I]IMP, respectively. To clarify involvement of the cerebral cortex, a three-dimensional surface display was created from the transaxial slices of SPECT early images using the STARCAM computer system.8 The threshold value to define the surface boundary was 55% of the global maximum counts in SPECT images. We adopted the threshold value because 11 control subjects without neurological diseases (mean age, 67.6±10.6 years) showed no defect in any cortical areas at 55% or lower threshold values.

Language Testing

Language abilities were assessed by evaluation of spontaneous speech, verbal comprehension, object naming, word repetition, and word reading, using the Standard Language Test of Aphasia in Japan.9 All aphasic patients presented with global aphasia, which was defined as severe disturbance of all language abilities. Although communicative abilities were considerably disturbed in these patients, in most instances they showed willingness to phonate or behave in response to the examiner’s commands. Language testing was performed more than 4 weeks after the onset in all cases. Two patients (patients 2 and 3) underwent reassessment of language testing 5 to 8 months after the onset.

Results

Lesion Sites

Distributions of the lesions in the 4 aphasic patients are illustrated in Fig 1. All aphasic patients had subcortical lesions in the putamen, posterior limb of the internal capsule, temporal isthmus, and periventricular white matter (PVWM). Two patients with infarction (patients 1 and 2) showed similar subcortical lesions in the globus pallidus (GP), putamen, and posterior internal capsule. The temporal isthmus and PVWM were also involved. One patient with hemorrhage (patient 3) showed subcortical lesions in the putamen, posterior internal capsule, temporal isthmus, and PVWM. The other patient with hemorrhage (patient 4) showed larger lesions, including the caudate nucleus, thalamus, putamen, GP, anterior and posterior internal capsule, and PVWM. The PVWM lesions of these patients extended from the anterior to the posterior part of the lateral ventricle. No cortical lesion was detectable in any aphasic patients. A right hemisphere lesion was found only in patient 4.

Distributions of the lesions in the 4 nonaphasic patients are illustrated in Fig 2. The lesion site in each patient was smaller than that in the aphasic group, but subcortical structures such as the putamen, GP, thalamus, internal capsule, and PVWM were also involved. In contrast with the aphasic group, the nonaphasic patients had no lesions in the temporal isthmus, and their PVWM lesions did not cover the entire length of the lateral ventricle.

Cerebral Blood Flow

The SPECT early images in all aphasic patients showed hypoperfusion in the left frontotemporal areas, extending from the posterior frontal region to the posterior temporal region (Fig 3). These hypoperfused areas included both cortical and subcortical structures. Two patients (patients 1 and 4) had larger hypoperfused areas extending to the parietal areas. There was no right hemisphere hypoperfusion except in patient 4, who had right parietal hypoperfusion. The SPECT delayed images in all aphasic patients demonstrated redistribu-
FIG 3. Early single-photon emission computed tomographic images of aphasic patients. All patients have hypoperfusion in the left frontotemporal areas.

FIG 4. Three-dimensional surface display of aphasic patients. All patients have cortical hypoperfusion, mainly in the perisylvian areas.

FIG 5. Three-dimensional surface display of nonaphasic patients. Perisylvian cortical areas are spared in each patient.

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ations of $[^{123}I]$IMP uptake. In 3 patients tracer reuptake was found in both the cortical and subcortical areas, but the other patient (patient 4) showed a decrease in tracer reuptake in the subcortical areas.

The SPECT early images in the nonaphasic group showed mainly left subcortical hypoperfusion. Two patients had no cortical hypoperfusion. The other two patients (patients 5 and 6) had less cortical hypoperfusion in the frontal and parietal cortices, respectively, than did the aphasic group. The SPECT delayed images in all nonaphasic patients demonstrated redistributions of the tracer with filling in both the subcortical and cortical areas.

Three-dimensional surface displays of all aphasic patients clearly demonstrated cortical hypoperfusion in the cortex of the convexity, centered on the left perisylvian areas (Fig 4). In patient 2, hypoperfusion was confined mainly to the inferoposterior frontal and superoposterior temporal cortices. In patient 3, hypoperfused areas were noted in the posterior frontal and entire temporal cortices. In patients 1 and 4, the larger hypoperfused areas formed an oval shape extending to the other parts of the frontal, temporal, and parietal cortices. All patients showed damage to the perisylvian language cortices such as Broca’s and Wernicke’s areas. The right hemisphere was spared, except in patient 4.

In the nonaphasic group, patient 5 had hypoperfusion in the left frontal cortex and patient 6 in the left parietal and temporal cortices. The other two patients had no cortical hypoperfusion. Perisylvian cortical hypoperfusion was undetectable in the nonaphasic group (Fig 5).

Language Abilities

The language abilities of each aphasic patient are shown in the Table. All patients presented with poor, nonfluent verbal output. Auditory comprehension of spoken words and sentences was severely disturbed in all patients. Visual comprehension of written words and sentences was also severely disturbed in 3 patients and moderately disturbed in the remaining patient (patient 3). Object naming was impossible in all patients. Repetition of words and sentences was impossible in patients 1 and 2 but was relatively preserved in patients 3 and 4. Oral reading was severely disturbed in 3 patients but was relatively preserved in a fourth patient (patient 3). The clinical features of patients 3 and 4 partly resembled mixed transcortical aphasia, but they had no
cal structures such as the caudate nucleus, putamen, or striatal aphasia or thalamic aphasia, follow subcortical bra. 1012 In our patients, however, global aphasia associated with cortical hypoperfusion persisted in the chronic stage, so the possibility appears to be negligible. The overall condition of their language abilities, however, remained in a state of global aphasia.

**Discussion**

The underlying mechanism of subcortical global aphasia remains to be clarified. The present study has provided some idea of the possible mechanism. Aphasic patients had larger subcortical lesions than did nonaphasic patients, and some subcortical structures involved in aphasic patients were spared in nonaphasic patients. The different patterns of subcortical involvement might be responsible for the different patterns of cortical perfusion found in the two groups. Aphasic patients had perisylvian cortical hypoperfusion, whereas nonaphasic patients had rather small hypoperfused cortical areas that spared the perisylvian language areas. Although 2 aphasic patients had larger hypoperfused areas extending to the other cortices, the remaining 2 patients with persistent global aphasia had mainly perisylvian cortical hypoperfusion. This fact raises the possibility that subcortical global aphasia is related to impairments of cortical functions, mainly in the perisylvian language areas.

Several possibilities arise concerning the mechanism underlying subcortical aphasia.10-12 The most plausible possibility is association with a cortical pathological lesion that is undetectable on CT scan. However, MRI in our 3 patients confirmed that the lesions were restricted to the subcortex only. In addition, redistribution of tracer uptake in cortical areas detected on SPECT delayed images might suggest functional changes rather than pathological changes in the cortex. Furthermore, some autopsied cases have been reported to show no pathological changes in the cortex.11 Thus, this explanation seems unlikely in our patients. Yet another theory is related to cortical dysfunction due to a mass effect or a vascular mechanism such as the ischemic penumbra.10-12 In our patients, however, global aphasia associated with cortical hypoperfusion persisted in the chronic stage, so the possibility appears to be negligible. Subcortical structures per se may play an important role in language functions.13,14 Aphasic syndromes, such as striatal aphasia or thalamic aphasia, follow subcortical stroke.3 In subcortical global aphasia, several subcortical structures such as the caudate nucleus, putamen, or GP have been variably involved. To our knowledge, however, patients with global aphasia variably have white matter lesions. Additionally, our nonaphasic patients also had subcortical nuclear lesions in the putamen, thalamus, and GP. Hence, even if subcortical structures do participate in language ability, global aphasia can hardly be attributed to subcortical nuclear lesions. As mentioned above, these possibilities seem unlikely in our patients, although some contribution of a pathological change in the cortex or a vascular mechanism, particularly in the early stage, cannot be completely ruled out.

Finally, a potential mechanism applicable to our patients involves the remote effect termed diaschisis, in which interruption of neural networks from a focal lesion induces depression of neural activities in a distant area of the brain. In line with this theory, white matter lesions have been proposed to be critical for subcortical aphasia.7,15 Regarding speech output, the subcallosal fasciculus and the anterior and middle one third of the PVWM are considered important. Regarding language comprehension, the role of the temporal isthmus and the posterior PVWM has been postulated. These areas contain fibers connecting the subcortex with the cortical language centers. In the present study all aphasic patients had white matter lesions in the temporal isthmus, PVWM, and posterior internal capsule. PVWM lesions covered almost the entire anteroposterior extent of the lateral ventricle. The subcallosal fasciculus was involved in only one patient (patient 4). In contrast, nonaphasic patients had smaller white matter lesions, mainly in the posterior internal capsule and PVWM. In the nonaphasic group the temporal isthmus was spared, and PVWM lesions did not encroach on the entire anteroposterior extent of the lateral ventricle. These results are consistent with the idea that white matter lesions play an important role in subcortical aphasia.7,11,12 In particular, the temporal isthmus and PVWM lesions interrupt neural circuits such as the corticocortical, geniculocortical, corticothalamic, and thalamocortical fibers, which are connected directly or indirectly with the perisylvian language areas. The interruption of neural circuits might lead to cortical hypometabolism and associated cortical hypoperfusion.10-12 Additionally, the pyramidal tract descending from the cortical mouth area is apt to be involved after damage to the internal capsule or PVWM. Thus, the severity of subcortical aphasia appears to depend on the distribution of white matter lesions. Both temporal isthmus lesions and large PVWM lesions might result in subcortical global aphasia.

<table>
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<th>Patient</th>
<th>Auditory Comprehension</th>
<th>Visual Comprehension</th>
<th>Object Naming</th>
<th>Repetition</th>
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Maximum score 30 40 20 15 15
Cortical hypoperfusion after subcortical stroke has also been reported in aphasic patients without global aphasia. In these studies, however, the precise anatomic distribution of cortical involvement related to aphasia was not clearly demonstrated. Another study showed that a patient with subcortical global aphasia had diffuse cortical hypometabolism in the left hemisphere, particularly in the temporoparietal region. In the present study three-dimensional surface displays showed cortical hypoperfusion, centered on the perisylvian areas, in all aphasic patients. The hypoperfused perisylvian cortices included both Broca’s and Wernicke’s areas. Two patients exhibited cortical hypoperfusion mainly in the perisylvian areas, but the other two patients had larger cortical hypoperfusion. The two patients with mainly perisylvian hypoperfusion had persistent global aphasia when reassessed more than 5 months later. Therefore, we consider that perisylvian cortical hypoperfusion is crucial for the development of subcortical global aphasia. Our findings support the idea that subcortical global aphasia is not strictly due to subcortical lesions and is associated with cortical involvement, particularly in the perisylvian language areas.

The question arises as to why severe aphasia occurs in a small proportion of patients with subcortical stroke. We cannot fully answer this question, but the following assumption seems applicable. Individual variations in the brain exist. From a morphological point of view, hemisphere asymmetry has been described to have an effect on recovery from aphasia. From a functional point of view, variations in plastic changes after damage to the brain should be regarded as a possible mechanism. The early occurrence and persistence of compensatory functions have been verified in animal studies. Individual functional reorganization in the cerebral cortex after subcortical stroke occurs in different patterns, and the compensatory strategy of the higher functions may vary from patient to patient. In the majority of cases interruption of neural connections with the perisylvian language areas may be fairly well compensated, but in some the damaged neural circuits related to language abilities may hardly be compensated.

References
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