# Subcortical Aphasia After Striatocapsular Infarction: Quantitative Analysis of Brain Perfusion SPECT Using Statistical Parametric Mapping and a Statistical Probabilistic Anatomic Map

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This study examined the relationship between the severity of aphasia and regional cerebral perfusion on brain SPECT using statistical parametric mapping (SPM) and a statistical probabilistic anatomic map (SPAM) in patients with a striatocapsular infarction (SCI) along with the other clinical and imaging findings. **Methods:** The subjects were 16 right-handed Korean-speaking patients with a left SCI who underwent $^{99m}$Tc-ethylcyteinate dimer ($^{99m}$Tc-ECD) SPECT (8.1 ± 4.8 d [mean ± SD] after onset). MRI showed that no patient had any abnormality in the cerebral cortex (6.8 ± 6.0 d after onset). The aphasia quotient (AQ), which is a measure of the severity of aphasia, was obtained by using the Korean version of the Western Aphasia Battery (5.3 ± 3.9 d after onset). For quantitative evaluation of cerebral perfusion, the asymmetry indices (AIs) for subcortical and cortical areas were calculated using SPM and SPAM. The infarct size was measured using MRI. **Results:** Aphasia occurred in 15 (2 global, 7 transcortical, and 6 anomic aphasia) of the 16 patients. Left cerebral cortical hypoperfusion was observed in all 15 patients with subcortical aphasia. Aphasia was more severe in 6 patients with extensive cerebral cortical hypoperfusion than in the remaining 10 patients (AQ = 41.8 ± 25.2 points vs. 84.2 ± 7.7 points [mean ± SD], $P = 0.001$). There was an association between the AQ and age ($\rho = -0.665$), infarct size ($\rho = -0.594$), AIs of the frontal cortex ($\rho = -0.653$), temporal cortex ($\rho = -0.782$), parietal cortex ($\rho = -0.694$), whole cerebral cortex ($\rho = -0.768$), and the cerebellar cortex ($\rho = 0.765$). Voxel-based SPM analysis showed a significant positive correlation between the AQ and the perfusion of the left temporal cortex and the right cerebellum. **Conclusion:** The severity of subcortical aphasia after a left SCI without cortical abnormalities on MRI is associated with the extent and severity of the left cerebral cortical hypoperfusion on brain perfusion SPECT performed during the subacute stage, particularly in the left temporal cortex. Quantitative brain perfusion SPECT using SPM and SPAM can help in evaluating subcortical aphasia in a SCI because it provides functional information that cannot be obtained by morphologic imaging.

**Key Words:** striatocapsular infarction; subcortical aphasia; brain perfusion SPECT; statistical parametric mapping; statistical probabilistic anatomic map

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Striatocapsular infarction (SCI) is a subtype of subcortical infarct involving the caudate nucleus, the putamen, and the anterior limb of the internal capsule (*1*). Although aphasia is traditionally designated as a cortical deficit, many studies have reported the occurrence of aphasia in patients with an isolated SCI without any evidence of cerebral cortical involvement (*1*). The underlying mechanism for subcortical aphasia after an isolated SCI is unclear. Several hypotheses have been proposed to explain the pathophysiology of subcortical aphasia: (a) the direct effect of the subcortical lesion, which suggests that the basal ganglia and internal capsule are essential components of the brain networks involved in the language function (*2*); (b) a disconnection of the cortical structures that are essential for language (*3*); (c) the impaired release of the language segments organized in the cortex into output (*4*); (d) the presence of diaschisis, where the subcortical lesion cuts off the neural input to a remote area of the brain, which leads to a dysfunction of the cortex with regard to the language function (*5*); and (e) cortical ischemic damage resulting from a combination of stenosis or an occlusion of the large cerebral vessels, sustained cortical hypoperfusion, and an incomplete cortical infarction that is not detected by anatomic imaging studies (*6–12*).

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Although it has been suggested that cortical hypoperfusion is one of the main causes of aphasia in a SCI, it is unclear if cortical hypoperfusion is due to diaschisis or to a true ischemic result caused by a large vessel stenosis or occlusion (*6–12*). Few studies have examined the association between the severity of aphasia and cortical hypoperfusion. In addition, most studies have used visual or quantitative analysis using a region-of-interest (ROI) method to correlate the brain perfusion imaging with subcortical aphasia (*13,14*). However, these methods are relatively subjective and are difficult to reproduce. Statistical parametric mapping (SPM), which is a voxel-based statistical method, is a well-known tool for identifying a cluster of voxels in brain imaging with a significant difference between patients and healthy control subjects or showing significant correlations with the other parameters. A statistical probabilistic anatomic map (SPAM) is an atlas-based volume of interest (VOI) that is used to obtain the regional counts from spatially normalized individual images into standardized brain templates. Both techniques provide objective and reproducible information for the regional abnormalities in cerebral perfusion and have been used recently and validated in various neurologic diseases but not in subcortical aphasia (*15–19*). The aim of this study was to examine the relationship between the severity of aphasia and regional cerebral perfusion on brain SPECT using SPM and SPAM in patients with a SCI along with the other clinical and imaging findings.

## MATERIALS AND METHODS

### Subjects

Thirty-three consecutive patients with a newly diagnosed SCI by brain MRI were initially enrolled in this study. The inclusion criteria are as follows: (a) SCI occurred in the dominant hemisphere without a history of a previous cerebral infarction; (b) no cerebral cortical involvement was found on the brain MRI, including the diffusion-weighted images; and (c) the brain perfusion SPECT and neuropsychologic tests, including an aphasia examination, were performed successfully during the subacute stage of the infarct. Overall, 16 right-handed subjects (8 men, 8 women; mean age, 64.8 ± 9.6 y [mean ± SD]; age range, 46–80 y) with a left SCI, who spoke Korean as their first language, were enrolled in this study. For SPM and SPAM analysis, the normal SPECT database from 16 neurologically healthy control subjects (8 men, 8 women; mean age, 70.7 ± 5.3 y; age range, 57–77 y) was used. The ethics committee of our institution approved the study protocol.

### Aphasia Examination

All patients underwent an aphasia examination using the Korean version of the Western Aphasia Battery (K-WAB) during the subacute stage of the SCI (5.3 ± 3.9 d [mean ± SD] after onset; range, 2–16 d) (*20,21*). The 4 subtests pertain to oral language: spontaneous speech (0–40 points), auditory comprehension (0–20 points), repetition (0–20 points), and naming (0–20 points). The severity of aphasia was evaluated by calculating the aphasia quotient (AQ) for each patient by summing the score of the 4 subtests. In the healthy control groups, AQ was reported to be 92.8 ± 4.2 points (*20,21*). In addition, the type of aphasia in each subject was determined (*20–22*).

### Brain MRI and MR Angiography

Brain MRI and MR angiography were performed on all subjects during the subacute stage of SCI (6.8 ± 6.0 d after onset; range, 1–20 d) using a 1.5-T MRI scanner (Signa; GE Healthcare).

Fast fluid-attenuated inversion recovery images, T1-weighted images, T2-weighted images, and diffusion-weighted images were obtained. All images were obtained during the same session and in the same orientation and slice positions. The diffusion-weighted images were acquired using a multislice, single-shot, spin-echo, echo-planar sequence with a repetition time of 6,500 ms and an echo time of 96.8 ms. Diffusion-weighted imaging was performed with a 128 × 128 matrix, a 28 × 28 cm field of view, a section thickness of 5 mm, and an intersection space of 2 mm. The size of the SCI was defined as the longest diameter noted on the diffusion-weighted images.

Three-dimensional time-of-flight MR angiography (repetition time/echo time, 55/6.9; 20° flip angle) was performed. The orientation of the volume slab was chosen to cover the circle of Willis, the posterior cerebral artery, and the middle cerebral artery. The slab thickness was 64 mm with 64 partitions, resulting in a section thickness of 1 mm. The acquisition matrix was 512 × 192 and the field of view was 22 cm. The occlusion or stenosis of the internal carotid artery and the major cerebral arteries was evaluated.

### Brain Perfusion SPECT

Brain perfusion SPECT using a 740-MBq dose of $^{99m}$Tc-ethylcysteinate dimer (ECD) and a triple-head γ-camera (Triad XLT; Trionix Research Laboratory) was performed on all subjects during the subacute stage of SCI (8.1 ± 4.8 d after onset; range, 1–19 d). The tomographic images were reconstructed using filtered backprojection with a Butterworth filter (cutoff frequency, 0.60 cycle/cm; order, 3) and were displayed in a 128 × 128 matrix (pixel size = 3.56 × 3.56 mm with a slice thickness of 3.56 mm). No attenuation correction was performed.

A rotational correction and centering in 3 dimensions of the SPECT dataset were performed; this was followed by realignment to the line between the bottom of the frontal cortex and the tentorial notch—that is, the gap between the cerebral cortex and the cerebellum on the SPECT images, which corresponds to the anterior commissure–posterior commissure line. The images were interpreted visually by the consensus of 2 nuclear medicine physicians who were unaware of the results of the aphasia examination and MRI. In this study, the presence of regional hypoperfusion in left frontal, temporal, and parietal cortices, right cerebellum, left basal ganglia, and left thalamus was visually assessed. Occipital cortex was excluded from the visual analysis because its perfusion is usually asymmetric (*23*). Regional hypoperfusion was defined as any degree of decreased perfusion compared with the perfusion of the symmetric contralateral region.

### SPM and SPAM Analyses

SPM2 software (Institute of Neurology, University of London, U.K.) implemented in Matlab 7.0 (Mathworks Inc.) was used for SPM and SPAM analysis. The SPECT images of the healthy control subjects and patients were spatially normalized to standard templates of the Montreal Neurological Institute (McGill University, Montreal, Quebec, Canada) by linear and nonlinear transformations (79 × 95 × 69 voxels; voxel size = 2 × 2 × 2 mm). The count of each voxel was normalized to the whole brain count using

the proportional scaling method to remove the effects of global intensity.

The SPAM images of the Montreal Neurological Institute consisting of 98 VOIs were used to objectively calculate the SPECT counts in the cerebral cortical, cerebellar, and subcortical VOIs (*15–18*). Each image consisted of the probabilities (0 ~ 1) that belong to specific regions. The SPAM probability-weighted mean counts of frontal cortex, temporal cortex, parietal cortex, occipital cortex, whole cerebral cortex, cerebellar cortex, basal ganglia, and thalamus per each hemisphere were obtained from the 98 VOIs using the probabilistic brain atlas, which were calculated by dividing the probability-weighted sum of all voxels in the VOI by the sum of the probability sum of the VOI and the number of voxels. The asymmetric index (AI) of the 8 brain regions was acquired using the following equation:

$$AI = (\text{SPAM probability-weighted mean counts of right VOIs} - \text{SPAM probability-weighted mean counts of left VOIs}) \times 200/(\text{SPAM probability-weighted mean counts of right VOIs} + \text{SPAM probability-weighted mean counts of left VOIs}).$$

For voxel-based analysis, the correlation between the SPECT data and the AQ was assessed using the "single-subject: covariates only"routine in SPM2. The AQ and cerebral regional perfusion are affected by the patient's age. Therefore, age was used as a variable to control for its potential confounding effect (*20,21,23*). The analysis threshold for the gray matter was 0.80. The voxels with a false discovery rate–corrected $P$ value $< 0.05$ were considered significant. Clusters with >20 continuous voxels (extent threshold, *Ke*) were considered to be of significant size. T-value maps of the significant voxels were overlaid on the 3-dimensionally rendered T1 MR template.

### Statistical Analysis

A Mann–Whitney $U$ test was used to compare the regional AIs between the healthy control subjects and the patients with a SCI and the AQ according to the presence of a cerebral artery occlusion or stenosis and brain perfusion abnormalities. The Spearman rank correlation test was used to correlate the AQ with the other clinical or imaging variables. $P < 0.05$ was considered significant.

## RESULTS

Table 1 shows the clinical characteristics of the patients and the results of imaging studies. Subcortical aphasia occurred in 15 of 16 subjects. Among the 16 subjects, MR angiography revealed occluded ($n = 5$) or stenotic ($n = 2$) horizontal segments of the left middle cerebral artery (M1) in 7 patients. There was no significant stenosis or occlusion of right cerebral, vertebral, and carotid arteries found in any of the patients. The AQ of 5 patients with an occluded M1 was significantly lower than that of the remaining 11 patients (39.4 ± 27.3 points vs. 81.4 ± 11.8 points, $P < 0.01$).

Visual analysis revealed left cerebral cortical hypoperfusion in 15 patients with aphasia (frontotemporoparietal in 6, temporal in 4, temporoparietal in 2, frontotemporal in 2, and parietal hypoperfusion in 1). The remaining 1 subject without aphasia showed no significant hypoperfusion on the cerebral cortices. Right cerebellar hypoperfusion was found in the 9 of 16 patients (56.3%). The AQ of the 6 patients with extensive cerebral cortical hypoperfusion was significantly lower than that of the remaining 10 patients (41.8 ± 25.2 points vs. 84.2 ± 7.7 points, $P = 0.001$). Among the 6 patients with extensive cerebral cortical hypoperfusion, 5 had an occluded M1 on MR angiography. Left thalamic hypoperfusion was noted in 9 of the 16 subjects. The AQ of

**TABLE 1**
Clinical Characteristics of Patients with Isolated SCI

| Patient no. | Age (y) | Sex | Aphasia type | AQ (points) | Infarct size (mm) | MRA | Regional asymmetric index on brain perfusion SPECT | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | F | T | P | O | Cx | Cb | BG | Th |
| 1 | 80 | F | Global | 6.8 | 38 | M1 occlusion | 3.42 | 2.93 | 10.11 | 0.58 | 5.72 | −4.23 | 27.21 | 9.63 |
| 2 | 75 | M | Global | 13.0 | 36 | M1 occlusion | 8.33 | 5.89 | 11.53 | 2.66 | 8.61 | −8.41 | 22.04 | 9.59 |
| 3 | 67 | M | TS | 53.4 | 37 | Normal | 2.78 | 3.46 | 7.34 | 5.26 | 5.40 | −4.26 | 43.38 | 3.14 |
| 4 | 64 | F | Mixed T | 54.0 | 28 | M1 occlusion | 3.34 | 4.81 | 12.47 | 3.49 | 6.92 | −4.03 | 28.79 | 4.22 |
| 5 | 67 | F | TS | 57.4 | 39 | M1 occlusion | 13.43 | 14.25 | 18.01 | 8.68 | 14.93 | 2.62 | 35.57 | 9.79 |
| 6 | 77 | F | Mixed T | 66.0 | 33 | M1 occlusion | 4.86 | 5.78 | 9.51 | −1.25 | 6.29 | −2.29 | 22.14 | 4.75 |
| 7 | 68 | M | Mixed T | 67.5 | 44 | Normal | 4.21 | 3.06 | 7.71 | −1.26 | 4.67 | −3.80 | 28.46 | 4.05 |
| 8 | 49 | M | TM | 79.2 | 30 | Normal | −0.27 | 0.95 | 6.55 | −0.49 | 2.15 | 0.52 | 34.00 | 3.92 |
| 9 | 68 | F | Anomic | 80.3 | 31 | Normal | 1.43 | −1.85 | 8.60 | 2.48 | 3.88 | −0.26 | 16.09 | 0.25 |
| 10 | 67 | M | TM | 81.6 | 28 | Normal | 2.10 | −4.10 | 5.20 | −2.68 | 1.46 | 0.83 | 18.06 | 1.17 |
| 11 | 75 | F | Anomic | 84.4 | 18 | M1 stenosis | −3.84 | −5.79 | 7.55 | 4.33 | 0.73 | 3.71 | 11.34 | −1.20 |
| 12 | 63 | F | Anomic | 86.8 | 22 | Normal | 4.18 | −1.41 | 8.86 | 1.69 | 4.84 | 0.80 | 28.08 | −1.39 |
| 13 | 46 | M | Anomic | 87.6 | 40 | Normal | 0.21 | 1.23 | 7.08 | 2.97 | 3.63 | −2.03 | 29.55 | 3.42 |
| 14 | 56 | M | Anomic | 88.8 | 11 | M1 stenosis | −2.88 | −4.56 | 7.44 | −1.02 | 0.65 | 1.62 | 11.25 | −3.71 |
| 15 | 56 | F | Anomic | 90.9 | 22 | Normal | −1.07 | −1.92 | 5.73 | 5.33 | 2.53 | 1.06 | 14.14 | −0.54 |
| 16 | 58 | M | Normal | 95.1 | 27 | Normal | 1.64 | −4.55 | 4.45 | 2.08 | 2.13 | 4.61 | 30.62 | 3.43 |

MRA = MR angiography; F = frontal cortex; T = temporal cortex; P = parietal cortex; O = occipital cortex; Cx = whole cerebral cortex; Cb = cerebellar cortex; BG = basal ganglia; Th = thalamus; M1 = horizontal segment of middle cerebral artery; TS = transcortical sensory; mixed T = mixed transcortical; TM = transcortical motor.

these 9 patients was significantly lower than that of the remaining 7 patients (56.7 ± 28.5 points vs. 83.3 ± 13.9 points, $P < 0.05$). SCI itself was seen as a focal perfusion defect on brain SPECT in all patients (Fig. 1). Figure 1 shows representative images of MRI and SPECT.

Figure 2 shows the differences in the regional AIs between the healthy control subjects and the patients with a SCI. All AIs of the patient group, except for the occipital cortex, were significantly higher than those of the healthy control subjects. This means that these patients had significant hypoperfusion on the left cerebral cortex, right cerebellar cortex, and left subcortical nuclei compared with the healthy control subjects.

Table 2 shows the correlations between the regional AI, AQ, infarct size, and age. The AQ showed a significant relationship with the age, infarct size, and AIs of the frontal cortex, parietal cortex, temporal cortex, cerebellar cortex, and whole cerebral cortex. The highest correlation was found between the AQ and AIs of the temporal cortex. There was a significant association between the infarct size and the AIs of the frontal cortex, temporal cortex, basal ganglia, thalamus, cerebellar cortex, and whole cerebral cortex. The highest correlation was found between the infarct size and the AI of the temporal cortex. The age of the subjects was associated with the AQ and AIs of the frontal cortex and parietal cortex.

Figure 3 shows the results of voxel-based SPM correlation analysis between the SPECT data and the AQ of each patient. Significant positive correlations were observed between the AQ and the perfusion of the left temporal cortex and right cerebellum. This means that the severity of subcortical aphasia was significantly associated with the severity of hypoperfusion in the left temporal cortex and right cerebellum.

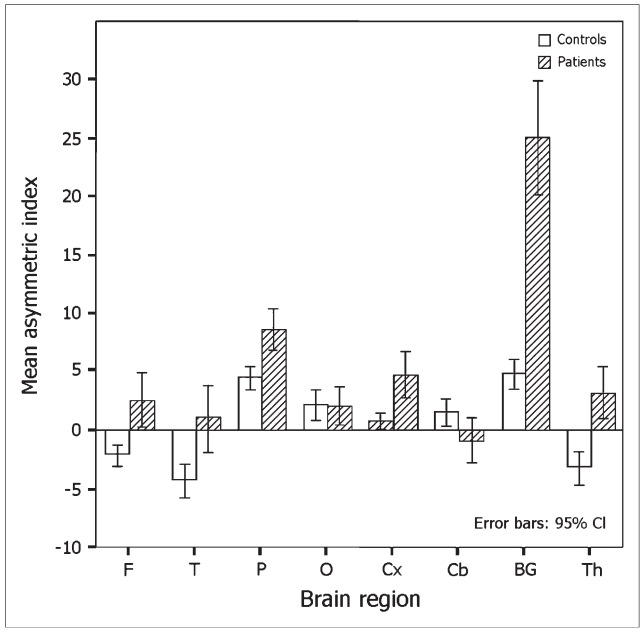


**FIGURE 2.** Comparisons of regional AIs between healthy control subjects and patients. F = frontal cortex; T = temporal cortex; P = parietal cortex; O = occipital cortex; Cx = whole cerebral cortex; Cb = cerebellar cortex; BG = basal ganglia; Th = thalamus; CI = confidence interval.

## DISCUSSION

These results suggest that the development and severity of aphasia in patients with a SCI without cortical involvement on MRI is closely related to the extent and severity of cerebral cortical hypoperfusion identified by brain perfusion SPECT. The severity of hypoperfusion in the left temporal cortex, which is responsible for the language function in right-handed subjects, showed the highest correlation

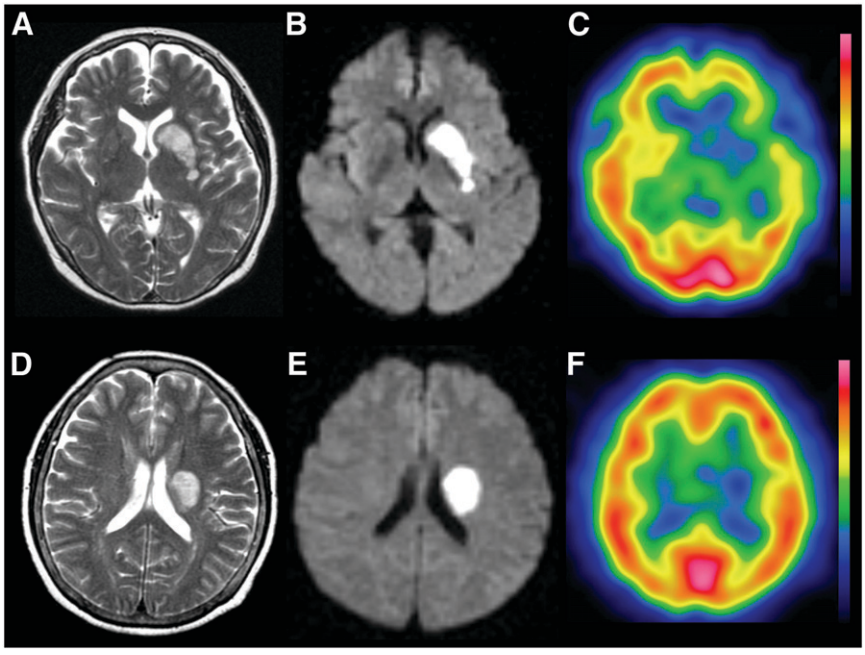


**FIGURE 1.** Representative images of T2-weighted MRI (A and D), diffusion-weighted MRI (B and E), and perfusion SPECT (C and F). (A–C) Patient with severe aphasia (AQ = 57.4 points) shows severe extensive left cerebral cortical hypoperfusion (AI of cerebral cortex = 14.93). (D–F) Another patient with mild aphasia (AQ = 90.9 points) had only mild hypoperfusion in left parietal cortex (AI of cerebral cortex = 2.53).

**TABLE 2**
Results of Correlation Analysis Between Regional AIs, AQ, Infarct Size, and Age

| AI | Mean ± SD | Range | Correlation with AQ | | Correlation with infarct size | | Correlation with age | |
|---|---|---|---|---|---|---|---|---|
| | | | ρ | *P* value | ρ | *P* value | ρ | *P* value |
| Frontal cortex | 2.62 ± 4.19 | −3.84 ~ 13.43 | −0.653 | <0.01 | 0.594 | <0.05 | 0.532 | <0.05 |
| Temporal cortex | 1.14 ± 5.21 | −5.79 ~ 14.25 | −0.782 | <0.001 | 0.729 | 0.001 | 0.379 | NS |
| Parietal cortex | 8.63 ± 3.30 | 4.45 ~ 18.01 | −0.694 | <0.005 | 0.328 | NS | 0.597 | <0.05 |
| Occipital cortex | 2.05 ± 3.01 | −2.68 ~ 8.68 | −0.053 | NS | 0.010 | NS | 0.321 | NS |
| Whole cerebral cortex | 4.66 ± 3.57 | 0.65 ~ 14.93 | −0.768 | 0.001 | 0.599 | <0.05 | 0.491 | NS |
| Cerebellar cortex | −0.85 ± 3.49 | −8.41 ~ 4.61 | 0.765 | 0.001 | −0.588 | <0.05 | −0.388 | NS |
| Basal ganglia | 25.05 ± 9.17 | 11.25 ~ 43.38 | −0.312 | NS | 0.560 | <0.05 | −0.206 | NS |
| Thalamus | 3.16 ± 4.04 | −3.71 ~ 9.79 | −0.721 | <0.005 | 0.713 | <0.005 | 0.453 | NS |
| Infarct size (mm) | 30 ± 9 | 11 ~ 44 | −0.594 | <0.05 | NA | NA | 0.311 | NS |
| Age (y) | 64.8 ± 9.6 | 46.4 ~ 79.6 | −0.665 | 0.005 | 0.311 | NS | NA | NA |

NS = not significant; NA = not applicable.

with the severity of aphasia on both SPM and SPAM analyses compared with the other clinical variables. The patients with an occluded left middle cerebral artery, on MR angiography, showed more severe aphasia and extensive severe cerebral cortical hypoperfusion when compared with other patients. This suggests that subcortical aphasia after an isolated SCI results from cortical ischemic damage and incomplete cortical infarction that is not detected by anatomic imaging studies (*6–12*).

Both SPM and SPAM analyses showed a significant correlation between the AQ and perfusion of the right cerebellum. No subjects had abnormalities in bilateral vertebral arteries on MR angiography and bilateral cerebellum on MRI. A significant negative correlation was found between the AIs of the cerebellum and the temporal cortex ($\rho = -0.618$, $P < 0.05$). A correlation coefficient between the AQ and AI of the cerebellum was lower than that between the AQ and AI of the temporal cortex (Table 2). Subcortical lesions may induce crossed cerebellar diaschisis on brain PET or SPECT (*24,25*). Therefore, a significant correlation between the AQ and perfusion of the right cerebellum might result from crossed cerebellar diaschisis secondary to left SCI and left cerebral cortical hypoperfusion.

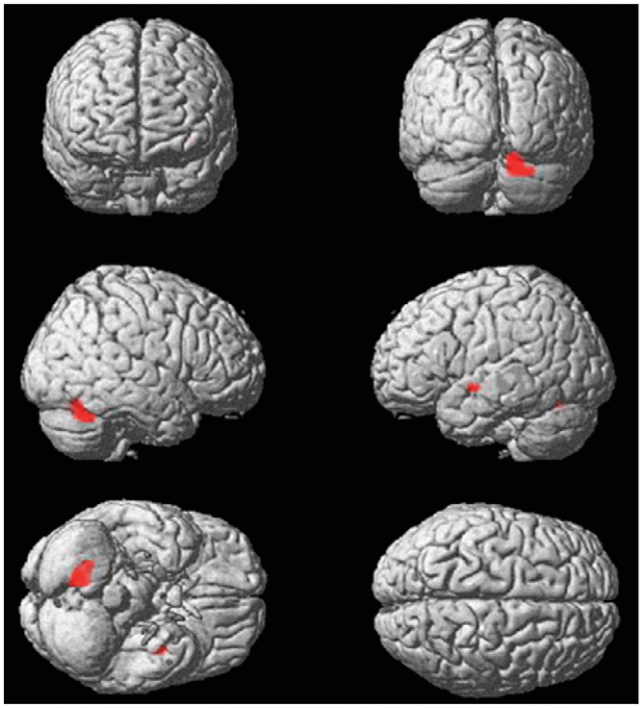

**FIGURE 3.** Voxel-based SPM analysis shows significant voxels on SPECT data to correlate with the AQ. Perfusion of left temporal cortex and right cerebellum was positively correlated with the AQ.

Left thalamic hypoperfusion was observed in 9 of 15 patients (60%) with subcortical aphasia. Aphasia was more severe in those patients with thalamic hypoperfusion than those without. The AI of the thalamus was also highly correlated with the AQ ($\rho = -0.721$), even though the correlation coefficient was lower than that of the temporal cortex. These results suggest that a thalamic disconnection in patients with SCI may contribute to the development of language deficits along with left temporal hypoperfusion (*1*).

The infarct size measured by the MR diffusion-weighted images showed significant correlations with the AQ and AIs of the frontal cortex, temporal cortex, whole cerebral cortex, cerebellar cortex, basal ganglia, and thalamus. However, all correlation coefficients of the infarct size with the AQ were lower than those of the AIs. This suggests that the severity of hypoperfusion on brain perfusion SPECT is more indicative of the severity of aphasia in patients with a SCI than the infarct size. The age of the subjects correlated with the AQ and AIs of the frontal cortex and parietal cortex. It was previously reported that the AQ decreased according to the age of healthy subjects (*20,21*). These results suggest that age also affects the language function in patients with subcortical aphasia. Age influences the regional brain perfusion (*23*). A voxel-based SPM analysis to remove the confounding effect of age showed a significant correlation only

between the AQ and the perfusion of the left temporal cortex. This suggests that hypoperfusion in the left temporal cortex may be the main pathophysiology of subcortical aphasia after a SCI irrespective of age.

Several imaging modalities have evaluated the association between subcortical aphasia after SCI and cortical hypoperfusion, including a $^{133}$Xe scan (*6*), $^{123}$I-hydroxyiodobenzylpropane diamine (HIPDM) SPECT (*5,7*), $^{123}$I-iodoamphetamine (IMP) (*9*), $^{99m}$Tc-hexamethylpropyleneamine oxime (HMPAO) SPECT (*8*), and MR perfusion-weighted imaging (*10,11*). Vallar et al. first reported an association between the severity of subcortical aphasia and cortical hypoperfusion on $^{123}$I-HIPDM SPECT (*7*). However, the number of subjects examined was quite small ($n$ = 6), and the etiology of subcortical aphasia varied and included both infarctions and hemorrhage. In addition, MRI was not performed. Hence, it is unclear if there are cerebral cortical abnormalities at the time of subcortical aphasia. MR perfusion-weighted images were also used to evaluate the subcortical aphasia (*10,11*). However, no quantitative analysis has been performed to associate the severity of aphasia with cortical hypoperfusion. In addition, the use of $^{123}$I-labeled brain perfusion agents such as HIPDM and IMP had high costs and limited availability compared with $^{99m}$Tc-labeled radiopharmaceuticals. Weiller et al. reported that subcortical aphasia in SCI occurred only in those patients with cortical hypoperfusion on $^{99m}$Tc-HMPAO SPECT (*8*). However, they did not perform quantitative analysis of SPECT data. In this study, quantitative analysis using SPM and SPAM of $^{99m}$Tc-ECD SPECT was adopted for the first time to evaluate subcortical aphasia after a SCI. $^{99m}$Tc-ECD SPECT may be a suitable imaging method for investigating subcortical aphasia after a SCI, considering the cost, availability, ability of quantitative analysis, and good correlations with the aphasia examination.

A recent study reported that a small cortical infarct identified by the MR diffusion-weighted images might contribute to the development of subcortical aphasia in patients with a SCI (*12*). However, although no patient with a SCI had cortical involvement identified by MR diffusion-weighted imaging, subcortical aphasia developed in most patients in this study. These findings suggest that brain perfusion SPECT might be more suitable for evaluating subcortical aphasia in a SCI than MR diffusion-weighted images.

The AQ of the K-WAB was used to evaluate the severity of aphasia in patients with a SCI for the first time (*20,21*). The WAB is one of a few standardized tools used for examining aphasia in English-speaking countries (*22*). The AQ in the WAB is widely used to examine the severity of aphasia in various disease states, such as dementia (*22,26*).

The K-WAB test has been validated previously elsewhere (*20,21*). In this study, the AQ showed a good correlation with the severity and extent of cerebral cortical hypoperfusion on brain SPECT. However, an aphasia examination is difficult to perform as a result of the patients' communication problems resulting from the SCI, which was one of major exclusion criteria in our study. In those patients, brain perfusion SPECT might be superior to the aphasia examination for making an accurate assessment because it is less affected by the patients' communication difficulties.

In this study, SPM and SPAM were used, to our knowledge, for the first time to make an objective and quantitative evaluation of brain perfusion SPECT in a SCI. Due to the process of special count normalization, a voxel-based statistical comparison of the brain images with different shapes is possible. The SPAM also enables an objective drawing and count evaluation of the VOIs in a reproducible manner. However, these methods have not been used widely in cerebrovascular diseases, such as infarction or ischemia, in which correct spatial normalization is difficult because they were originally developed for neurocognitive studies, where brains have a normal structure (*17,19*). The correct spatial normalization of all SPECT data was verified using the "Check Reg" routine in SPM2. The results were quite consistent with the previous studies (*6–12*). This may be possible because none of the subjects had cerebral cortical abnormalities on MRI except for the unilateral striatocapsular lesion. We used the AI to evaluate the severity and extent of hypoperfusion on SPECT. Although no significant abnormalities were found in the right cerebral hemisphere or the corpus callosum, clinically or on MRI and MR angiography, we cannot exclude the possibility of accompanying interhemispheric disconnection after a SCI, which might induce bilateral perfusion abnormalities and affect the AI. The small number of patients enrolled is another limitation. Because of the retrospective design, brain perfusion SPECT was not performed on all subjects initially diagnosed with a SCI. In addition, patients who could not complete the aphasia examination due to communication difficulties were excluded from the study. Further studies with a larger number of subjects will be needed to confirm these findings and to specify the role of left temporal hypoperfusion for evaluating the development and prognosis of subcortical aphasia.

## CONCLUSION

Subcortical aphasia after a left SCI without cortical abnormalities on MRI is associated with left cerebral cortical hypoperfusion on brain perfusion SPECT performed during the subacute stage, particularly in the left temporal cortex. The severity of aphasia is closely related to the extent and severity of cortical hypoperfusion. Quantitative brain perfusion SPECT using SPM and SPAM may be helpful for evaluating subcortical aphasia in a SCI as it provides functional information that cannot be obtained by morphologic imaging.

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