Postoperative Cortical Neural Loss Associated With Cerebral Hyperperfusion and Cognitive Impairment After Carotid Endarterectomy

Kohei Chida, MD; Kuniaki Ogasawara, MD; Yasunori Suga, MD; Hideo Saito, MD; Masakazu Kobayashi, MD; Kenji Yoshida, MD; Yasunari Otawara, MD; Akira Ogawa, MD

Background and Purpose—Although cerebral hyperperfusion after carotid endarterectomy (CEA) often impairs cognitive function, MRI does not always demonstrate structural brain damage associated with postoperative cognitive impairment. The purpose of the present study was to determine whether postoperative cortical neural loss, which can be detected by 123I-iomazenil single-photon emission CT, is associated with cerebral hyperperfusion after CEA and whether it correlates with postoperative cognitive impairment.

Methods—In 60 patients undergoing CEA for ipsilateral internal carotid artery stenosis (>70%), cerebral blood flow was measured using N-isopropyl-p-[123I]-iodoamphetamine single-photon emission CT before and immediately after CEA and on the third postoperative day. The distribution of benzodiazepine receptor binding potential in the cerebral cortex was assessed using 123I-iomazenil single-photon emission CT before and 1 month after surgery and was analyzed using 3-dimensional stereotactic surface projection. Neuropsychological testing was also performed preoperatively and at the first postoperative month.

Results—Post-CEA hyperperfusion and postoperative cognitive impairment were observed in 9 patients (15%) and 8 patients (13%), respectively. Post-CEA hyperperfusion was significantly associated with postoperative hemispheric reduction of benzodiazepine receptor binding potential (95% CIs, 2.765 to 148.804; \( P = 0.0031 \)). Post-CEA hyperperfusion (95% CIs, 1.183 to 229.447; \( P = 0.0370 \)) and postoperative hemispheric reduction of benzodiazepine receptor binding potential (95% CIs, 1.003 to 77.381; \( P = 0.0496 \)) were also significantly associated with postoperative cognitive impairment.

Conclusions—Cerebral hyperperfusion after CEA results in postoperative cortical neural loss that correlates with postoperative cognitive impairment. (Stroke. 2009;40:448–453.)

Key Words: carotid endarterectomy ■ cerebral hyperperfusion ■ cognitive impairment ■ neural loss
cortical benzodiazepine receptor binding indicates cortical neural damage or loss.\textsuperscript{10,11}\textsuperscript{12}

The purpose of the present study was to determine whether postoperative cortical neural loss, which can be detected by $^{123}$I-IMZ SPECT, is associated with cerebral hyperperfusion after CEA and whether it correlates with postoperative cognitive impairment.

**Methods**

**Subjects**

Sixty patients with ipsilateral internal carotid artery (ICA) stenosis ($\geq 70\%$) and useful residual function (modified Rankin disability scale 0, 1, or 2) who underwent CEA were enrolled in the present study. Fifty-six of the 60 patients were men and 4 were women. Mean age of the patient population was 68.6 $\pm$ 6.8 years (mean $\pm$ SD), ranging from 44 to 78 years. Concomitant disease states and symptoms were recorded, including 52 patients with hypertension, 21 patients with diabetes mellitus, and 31 patients with hyperlipidemia. Thirty-seven patients evinced ipsilateral carotid territory symptoms, including 11 patients with transient ischemic attacks, 6 patients with transient ischemic attacks and subsequent stroke, and 20 patients with stroke alone. Twenty-three patients had asymptomatic ICA stenosis. Preoperative MRI, including diffusion-weighted sequences, demonstrated infarction in the hemisphere ipsilateral to the ICA stenosis in 35 patients and no infarction in 25 patients. All patients underwent preoperative angiography with arterial catheterization. Overall average degree of ICA stenosis was 85.9$\%$ with a range of 70$\%$ to 99$\%$ according to the method of the North American Symptomatic Carotid Endarterectomy Trial.\textsuperscript{13} The contralateral ICA was occluded in 5 patients, and 7 additional patients had 60$\%$ to 95$\%$ stenosis.

This study was reviewed and approved by the institutional ethics committee. Written informed consent was obtained from all subjects or their next of kin.

**Single-Photon Emission CT**

SPECT studies were performed using a ring-type SPECT scanner (Headsetome-SET080; Shimadzu Corp, Kyoto, Japan), which provided 31 tomographic images simultaneously. The spatial resolution of the scanner with a low-energy, all-purpose collimator was 13 mm full width at half maximum at the center of the field of view, and the slice thickness was 25 mm full width at half maximum at the field of view center. Image slices were taken at 5 mm center-to-center spacing parallel to the orbitomeatal line. The images were reconstructed using the weighted-filtered backprojection technique, in which the attenuation correction was made by detecting the edge of the object. An attenuation coefficient of 0.065 cm$^{-1}$, a Butterworth filter (cutoff=0.45 cycle/cm; order=3), and a ramp filter were used for image reconstruction.

CBF was assessed using $N$-isopropyl-$p$-$[^{123}]$-iodoamphetamine and SPECT before and immediately after CEA. In addition, patients with post-CEA hyperperfusion underwent a third CBF measurement in the same manner 3 days after CEA. The $N$-isopropyl-$p$-$[^{123}]$-iodoamphetamine SPECT study was performed as described previously,\textsuperscript{14,15} and the quantitative CBF images were calculated according to the $N$-isopropyl-$p$-$[^{123}]$-iodoamphetamine-autoradiography method.\textsuperscript{16,17}

The distribution of benzodiazepine receptor binding potential in the cerebral cortex was assessed using $^{123}$I-IMZ SPECT before and 1 month after surgery. An intravenous injection of approximately 167 Mbi $^{123}$I-IMZ was administered after a 1-minute infusion of physiological saline at a rate of 20 mL/min. One hundred eighty minutes later, scans were initiated with a scanning duration of 23 minutes.\textsuperscript{11,12}

All $N$-isopropyl-$p$-$[^{123}]$-iodoamphetamine and $^{123}$I-IMZ SPECT image data were transferred to a personal computer and converted to a binary format. Stereotactic normalization was performed to transform images into a standardized 15 964 pixels using 3-dimensional stereotactic surface projection (NEUROSTAT).\textsuperscript{16} In $N$-isopropyl-$p$-$[^{123}]$-iodoamphetamine SPECT images, the ratio of postoperative CBF to preoperative CBF was calculated for each pixel. A pixel with a ratio $>2.0$ (postoperative CBF increase $>100\%$ compared with preoperative values) was designated as representing hyperperfusion.\textsuperscript{1}

Furthermore, the ratio ($\%$) of the number of pixels with hyperperfusion in the cerebral hemisphere ipsilateral to CEA to the total number of pixels of the entire unilateral cerebral hemisphere (7982 pixels) was calculated. When this ratio was $>50\%$, the patient was defined as having cerebral hyperperfusion.

In each pixel in $^{123}$I-IMZ SPECT images, the asymmetry index (AI) was calculated as the following formula: $AI=(C_{CCEA}-C_{CCON})/((C_{CCEA}+C_{CCON}))\times 100$, where $C_{CEA}$ is the count on the pixel ipsilateral to CEA and $C_{CON}$ is the count on the corresponding pixel on the contralateral side. The AIs were calculated before and after surgery, and the difference between the AIs (postoperative values $-$ preoperative values) was calculated and defined as $\Delta AI$. As controls, 20 healthy volunteers (20 men; age range, 30 to 50 years; mean age, 38 years) underwent 2 separate IMZ SPECT studies in the same manner. The interval between the 2 studies ranged from 1 month to 2 months. The 20 healthy volunteers were assigned into one of 2 groups, each consisting of 10 subjects. In the first group of healthy volunteers, $\Delta AI$ in each pixel was calculated when the left or right cerebral hemispheres was defined as the CEA side, respectively. As a result, the mean $\pm$ 2 SDs of $\Delta AI$ was 0.0 to $-5.0$ in 8914 pixels (56%), $-5.0$ to $-10.0$ in 4267 pixels (27%), $-10.0$ to $-20.0$ in 2379 pixels (15%), and $<-20.0$ in 404 pixels (2%) of a total of 15 964 pixels. In each pixel in each patient, $\Delta AI$ less than the mean $-2.0$ SDs of the value in the first group of healthy volunteers was defined as postoperatively reduced benzodiazepine receptor binding potential (BRBP). In each patient, the number of pixels with postoperatively reduced BRBP in the cerebral hemisphere ipsilateral to CEA was calculated, and the ratio ($\%$) of the number of pixels with reduced BRBP to a total number of pixels of the entire unilateral cerebral hemisphere (7982 pixels) was calculated and defined as the area with postoperatively reduced BRBP. Furthermore, in the second group of healthy volunteers, the area with postoperatively reduced BRBP was calculated using this definition based on data in the first group of healthy volunteers; the area was 4.0$\%$ $\pm$ 2.2$\%$ (mean $\pm$ SD) or 3.8$\%$ $\pm$ 2.1$\%$ when the left or right cerebral hemispheres was defined as the CEA side, respectively. When a patient had an area with postoperatively reduced BRBP more than the mean $+2.0$ SDs of the value (8.4$\%$ in the left hemisphere or 8.0$\%$ in the right hemisphere), the patient was defined as having postoperative hemispheric reduction of BRBP.

**Intraoperative and Postoperative Management**

All patients underwent surgery under general anesthesia. An intraluminal shunt duringICA clamping was not used in any of the patients. The mean duration of ICA clamping was 36 minutes, ranging from 27 to 49 minutes.

In patients with post-CEA hyperperfusion, intensive control of arterial blood pressure between 100 and 140 mm Hg was instituted using intravenous administration of antihypertensive drugs immediately after CEA. When CBF decreased and hyperperfusion was resolved on the third postoperative day, pharmacological control of blood pressure was discontinued. However, when hyperperfusion persisted, systolic arterial blood pressure was maintained below 140 mm Hg. When hyperperfusion syndrome developed, the patient was placed in propofol coma. A diagnosis of hyperperfusion syndrome required: (1) seizure, deterioration of consciousness level, and/or development of focal neurological signs such as motor weakness; and (2) hyperperfusion on the SPECT performed after CEA.

All patients underwent diffusion-weighted MRI (DWI) 1 day after surgery. Patients with cerebral hyperperfusion on CBF imaging performed immediately after surgery also underwent MRI on the third postoperative day and the first postoperative month. Furthermore, patients with cerebral hyperperfusion syndrome underwent additional MRI on the day on which symptoms developed.

**Neuropsychological Evaluation**

A battery of neuropsychological tests was administered, consisting of the Japanese translation of the Wechsler Adult Intelligence Scale.
Revised (WAIS-R), the Japanese translation of the Wechsler Memory Scale, and Rey-Osterreith Complex Figure test (Rey test). WAIS-R provides measures of general intellectual function and generates a verbal and performance intelligence quotient (IQ). Wechsler Memory Scale assesses orientation, recall of current information, recall of passages, sustained attention, digit span, and new learning of associative word pairs. The Rey test evaluates constructional ability and visual memory. The subtests within the Rey test include the copy trial, in which the subject copies a drawing of a complex figure, and a recall trial, in which the subject draws the figure from memory after a 30- to 45-minute delay. Thus, 5 scores (WAIS-R verbal IQ, WAIS-R performance IQ, Wechsler Memory Scale, Rey copy, and Rey recall) were used to evaluate cognitive function.

The neuropsychological tests were performed before and 1 month after surgery. All examinations were administered by a trained neuropsychologist who was blinded to the patients’ clinical information.

As controls, 44 patients with asymptomatic unruptured cerebral aneurysms (17 men and 27 women; 32 to 70 years of age; mean age, 56.8 years) underwent the same neuropsychological tests before and 1 month after neck clipping through craniotomy. None of the 44 patients had new postoperative neurological deficits and brain injury caused by surgery for the aneurysms on postoperative CT. Differences in each neuropsychological test score before and after neck clipping (postoperative scores—preoperative scores) were 2.4±4.6 (mean±SD) in the WAIS-R verbal IQ, 4.8±5.2 in the WAIS-R performance IQ, 2.9±8.1 in the Wechsler Memory Scale, 0.2±1.1 in the Rey copy, and 2.6±4.2 in the Rey recall. Thus, the mean −2 SD of the differences was −6.8 for the WAIS-R verbal IQ, −5.6 for the WAIS-R performance IQ, −13.3 for the Wechsler Memory Scale, −2.0 for the Rey copy, and −5.8 for the Rey recall. For the neuropsychological test scores of each patient undergoing CEA, a deficit was defined as a postoperative test score more than the absolute value of the mean −2 SDs of the difference less than the preoperative score. A patient was considered as having postoperative cognitive impairment when the patient had one or more postoperative neuropsychological scores with a deficit.

Statistical Analysis
Data are expressed as the mean±SD. The relationship between the area with postoperatively reduced BRBP and post-CEA hyperperfusion or postoperative cognitive impairment was evaluated using the Mann-Whitney U test. The relationship between each variable and postoperative hemispheric reduction of BRBP or postoperative cognitive impairment was evaluated by univariate analysis using the Mann-Whitney U test or χ² test. A multivariate statistical analysis of factors related to postoperative hemispheric reduction of BRBP or postoperative cognitive impairment was also performed using a logistic regression model. Variables with P<0.2 in the univariate analyses were selected for analysis in the final model. Differences were deemed statistically significant if P<0.05.

Results
All patients recovered within 1 hour after surgery without new major neurological deficits. DWI performed 1 day after surgery showed new hyperintense lesions in the cerebral hemisphere ipsilateral to CEA in 14 (23%) of the 60 patients studied when compared with preoperative DWI. The diameter of all new hyperintense lesions was ≤1.5 cm.

Post-CEA hyperperfusion on SPECT imaging was observed in 9 patients (15%). In 7 of these 9 patients, hyperperfusion resolved in the SPECT performed on the third postoperative day, and pharmacological control of blood pressure was discontinued. These patients did not experience new neurological symptoms eventually. The remaining 2 patients with post-CEA hyperperfusion experienced a progressive increase in CBF on the third postoperative day and developed hyperperfusion syndrome. One of these patients experienced motor weakness of the upper and lower extremities in the side contralateral to surgery on the seventh postoperative day. Another patient experienced focal seizures as evidenced by motor disturbances of the upper extremity in the side contralateral to surgery 6 days after surgery. Coma was induced in these 2 patients. After termination of the propofol coma, these patients eventually experienced full recovery. None of the 9 patients with post-CEA hyperperfusion exhibited new lesions on MRI performed on the third postoperative day, the day on which symptoms developed, or at the first postoperative month.

The area with postoperatively reduced BRBP ranged from 1.7% to 14.5% (5.5%±2.8%) among the 60 patients studied. The area was significantly larger in patients with postoperative hyperperfusion than in those without (P=0.0001) and was significantly larger in patients with postoperative cognitive impairment than in those without (P=0.0001). Closed and open circles indicate patients with and without postoperative cognitive impairment, respectively. Arrows indicate patients with cerebral hyperperfusion syndrome.

Figure 1. Relationship between area with postoperatively reduced BRBP, postoperative hyperperfusion, and postoperative cognitive impairment. The area was significantly larger in patients with postoperative hyperperfusion than in those without (P=0.0001) and was significantly larger in patients with postoperative cognitive impairment than in those without (P=0.0001). Closed and open circles indicate patients with and without postoperative cognitive impairment, respectively. Arrows indicate patients with cerebral hyperperfusion syndrome.
higher in patients with postoperative hemispheric reduction of BRBP than in those without. Other variables were not significantly associated with postoperative hemispheric reduction of BRBP. After eliminating variables that were closely related to others, the following items with \( P < 0.2 \) in the univariate analyses were adopted as confounders in the logistic regression model for the multivariate analysis: hypertension, symptomatic lesion, infarction on preoperative MRI, degree of ICA stenosis, and postoperative hyperperfusion. The analysis revealed that only postoperative hyperperfusion was significantly associated with postoperative hemispheric reduction of BRBP (95% CIs, 2.765 to 148.804; \( P = 0.0031 \)).

At the postoperative neuropsychological assessment, 8 patients (13%) showed postoperative cognitive impairment. The area with postoperatively reduced BRBP was significantly larger in patients with postoperative cognitive impairment (9.7% ± 3.0%) than in those without (4.9% ± 2.1%; \( P = 0.0001 \); Figure 1). Results of univariate analysis of factors related to postoperative cognitive impairment are summarized in Table 2. The incidences of post-CEA hyperperfusion and postoperative hemispheric reduction of BRBP were significantly higher in patients with postoperative cognitive impairment than in those without.

### Table 1. Univariate Analysis of Factors Related to Postoperative Hemispheric Reduction of BRBP

<table>
<thead>
<tr>
<th>Variables</th>
<th>Yes (n=11)</th>
<th>No (n=49)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean±SD</td>
<td>69.3±5.8</td>
<td>68.4±7.1</td>
<td>0.7084</td>
</tr>
<tr>
<td>Male gender</td>
<td>11 (100%)</td>
<td>45 (92%)</td>
<td>&gt;0.9999</td>
</tr>
<tr>
<td>Hypertension</td>
<td>8 (73%)</td>
<td>44 (90%)</td>
<td>0.1538</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>4 (36%)</td>
<td>27 (55%)</td>
<td>&gt;0.9999</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>4 (36%)</td>
<td>27 (55%)</td>
<td>0.3271</td>
</tr>
<tr>
<td>Symptomatic lesion</td>
<td>9 (82%)</td>
<td>28 (57%)</td>
<td>0.1778</td>
</tr>
<tr>
<td>Infarction on preoperative MRI</td>
<td>9 (82%)</td>
<td>26 (53%)</td>
<td>0.1010</td>
</tr>
<tr>
<td>Degree of ICA stenosis, %, mean±SD</td>
<td>90.5±5.7</td>
<td>84.8±9.0</td>
<td>0.0455</td>
</tr>
<tr>
<td>Bilateral lesions</td>
<td>9 (82%)</td>
<td>39 (80%)</td>
<td>&gt;0.9999</td>
</tr>
<tr>
<td>Duration of ICA clamping, minutes, mean±SD</td>
<td>37±6</td>
<td>36±5</td>
<td>0.4847</td>
</tr>
<tr>
<td>New ischemic lesions on DWI on the first postoperative day</td>
<td>3 (27%)</td>
<td>11 (22%)</td>
<td>0.7075</td>
</tr>
<tr>
<td>Postoperative hyperperfusion</td>
<td>6 (55%)</td>
<td>3 (6%)</td>
<td>0.0006</td>
</tr>
</tbody>
</table>

### Table 2. Univariate Analysis of Factors Related to Postoperative Cognitive Impairment

<table>
<thead>
<tr>
<th>Variables</th>
<th>Yes (n=8)</th>
<th>No (n=52)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean±SD</td>
<td>70.4±5.2</td>
<td>68.3±7.0</td>
<td>0.4318</td>
</tr>
<tr>
<td>Male gender</td>
<td>7 (88%)</td>
<td>71 (94%)</td>
<td>&gt;0.9999</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5 (63%)</td>
<td>47 (90%)</td>
<td>0.0648</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3 (38%)</td>
<td>18 (35%)</td>
<td>&gt;0.9999</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>4 (50%)</td>
<td>27 (52%)</td>
<td>&gt;0.9999</td>
</tr>
<tr>
<td>Symptomatic lesion</td>
<td>6 (75%)</td>
<td>31 (60%)</td>
<td>0.6983</td>
</tr>
<tr>
<td>Infarction on preoperative MRI</td>
<td>6 (73%)</td>
<td>29 (56%)</td>
<td>0.4493</td>
</tr>
<tr>
<td>Degree of ICA stenosis, %, mean±SD</td>
<td>88.8±7.4</td>
<td>85.4±8.9</td>
<td>0.2412</td>
</tr>
<tr>
<td>Bilateral lesions</td>
<td>7 (88%)</td>
<td>41 (79%)</td>
<td>&gt;0.9999</td>
</tr>
<tr>
<td>Duration of ICA clamping, minutes, mean±SD</td>
<td>37±6</td>
<td>36±5</td>
<td>0.7937</td>
</tr>
<tr>
<td>New ischemic lesions on DWI on the first postoperative day</td>
<td>2 (25%)</td>
<td>12 (23%)</td>
<td>&gt;0.9999</td>
</tr>
<tr>
<td>Postoperative hyperperfusion</td>
<td>5 (63%)</td>
<td>4 (8%)</td>
<td>0.0011</td>
</tr>
<tr>
<td>Postoperative hemispheric reduction of BRBP</td>
<td>6 (75%)</td>
<td>5 (10%)</td>
<td>0.0002</td>
</tr>
</tbody>
</table>
impairment than in those without. Other variables were not significantly associated with postoperative cognitive impairment. After eliminating variables that were closely related to others, the following items with \( P < 0.2 \) in the univariate analyses were adopted as confounders in the logistic regression model for the multivariate analysis: hypertension, post-CEA hyperperfusion, and postoperative hemispheric reduction of BRBP. The analysis revealed that post-CEA hyperperfusion (95% CIs, 1.183 to 229.447; \( P = 0.0370 \)) and postoperative hemispheric reduction of BRBP (95% CIs, 1.003 to 77.381; \( P = 0.0496 \)) were significantly associated with postoperative cognitive impairment.

Figure 2 shows SPECT images in one patient with cerebral hyperperfusion syndrome and cognitive impairment after surgery.

**Discussion**

Previous studies have demonstrated that patients with asymptomatic cerebral hyperperfusion on CBF imaging do not exhibit new postoperative lesions on MRI and that even the reversible vasogenic or cytotoxic edema on MRI develops in less than half of patients with cerebral hyperperfusion syndrome.\(^8\)\(^,\)\(^21\) This is consistent with results from the present study.

\(^{123}\)I-IMZ SPECT images in the present study displayed \(^{123}\)I-IMZ uptake in the cerebral cortex at 180 minutes after intravenous injection of the tracer. Investigators have demonstrated that these images are proportional to the distribution of benzodiazepine receptor binding potential.\(^10\)\(^–\)\(^12\) In addition, post-CEA hyperperfusion often develops in the ipsilateral cerebral cortex but not in the contralateral cerebral cortex.\(^6\) Thus, a significant postoperative reduction of \(^{123}\)I-IMZ uptake in the ipsilateral cerebral cortex relative to that in the contralateral cerebral cortex was defined as postoperatively reduced BRBP in the ipsilateral cerebral cortex. As a result, the area with postoperatively reduced BRBP was significantly larger in patients with post-CEA hyperperfusion than in those without, and post-CEA hyperperfusion was significantly associated with postoperative hemispheric reduction of BRBP. In addition, in all patients with post-CEA hyperperfusion, 80% or more of the pixels with postoperatively reduced BRBP exhibited hyperperfusion. These data suggest that cerebral hyperperfusion after CEA results in postoperative cortical neural loss and support the hypothesis that \(^{123}\)I-IMZ SPECT can detect neuronal damage that CT or MRI cannot.\(^10\)\(^–\)\(^12\)

Postoperative cortical neural loss may also occur through other mechanisms. For example, a significant number of patients have evidence of gaseous and particulate emboli in the middle cerebral artery during CEA.\(^22\) In addition, new ischemic lesions on DWI performed within a few days after surgery are seen in approximately 10% of patients undergoing CEA, and the number of embolic signals on transcranial Doppler ultrasonography high-intensity transient signal analysis generated during CEA is strongly correlated with postoperative evidence of new hyperintense lesions on DWI.\(^23\) In the present study, although DWI performed 1 day after surgery showed new ischemic lesions in the cerebral hemisphere ipsilateral to CEA in 23% of patients, the presence or absence of the lesions was not associated with postoperative hemispheric reduction of benzodiazepine receptor binding potential. Postoperative cortical neural loss may occur secondary to hemispheric hyperperfusion during CEA. Clamping of the carotid arteries during CEA results in a transient decrease in CBF in the ipsilateral middle cerebral artery territory in many patients.\(^2\) If the change in hemispheric CBF is significant enough to damage the cortical neurons, it may result in postoperative hemispheric reduction of benzodiazepine receptor binding potential. In the present study, the duration of ICA clamping was not associated with postoperative hemispheric reduction of benzodiazepine receptor binding potential, but the intensity of hyperperfusion during ICA clamping was not examined.

Cognitive impairment occurs in 10% to 30% of patients after CEA,\(^7\)\(^,\)\(^24\) and postoperative cerebral hyperperfusion is associated with impairment of cognitive function.\(^7\)\(^,\)\(^24\) However, MRI does not always demonstrate structural brain damage associated with postoperative cognitive impairment,\(^8\) which is consistent with results from the present study. By contrast, the area with postoperatively reduced BRBP was significantly larger in patients with postoperative cognitive impairment than in those without, and postoperative hemispheric reduction of BRBP was significantly associated with postoperative cognitive impairment. These findings suggest that cortical neural loss after CEA correlates with postoperative cognitive impairment and is consistent with previous findings that the degree of the decrease in benzodiazepine receptor binding is associated with the presence or absence of neurological symptoms.\(^12\)

A recent study investigated the significance of postoperative crossed cerebellar diaschisis in patients with post-CEA hyperperfusion.\(^25\) In that study, although crossed cerebellar diaschisis developed on the third postoperative day in patients that resulted in postoperative cognitive impairment associated with cerebral hyperperfusion, patients who developed post-CEA hyperperfusion without exhibiting subsequent crossed cerebellar diaschisis did not experience postoperative cognitive impairment. These findings suggest that post-CEA hyperperfusion-mediated reductions in cerebral metabolism result in cerebral dysfunction and cognitive impairment,\(^25\) which is also consistent with observations from the present study.

The present study possesses several limitations that require discussion. First, IMZ SPECT images were analyzed on a pixel-by-pixel basis using 3-dimensional stereotactic surface projection, and \( \Delta AI \) with a value less than the mean \(-2 \) SDs in the healthy volunteers was defined as postoperatively reduced BRBP. According to this definition, the threshold was less than \(-10.0 \) in 17% of a total of pixels. Thus, postoperatively reduced BRBP may be underestimated in this study.

Second, although neuropsychological tests are regarded as good measures of postoperative cognitive impairment,\(^7\)\(^,\)\(^24\) the criterion for defining a significant impairment in neuropsychological test can vary. Heyer et al\(^24\) assessed patients undergoing CEA and lumbar spine surgery with a battery of pre- and postoperative neuropsychological tests and defined patients undergoing spine surgery as a control group. Fur-
Cortical Neural Loss After CEA

Chida et al

Disclosures

None.

References

Postoperative Cortical Neural Loss Associated With Cerebral Hyperperfusion and Cognitive Impairment After Carotid Endarterectomy: 123I-iomazenil SPECT Study
Kohei Chida, Kuniaki Ogasawara, Yasunori Suga, Hideo Saito, Masakazu Kobayashi, Kenji Yoshida, Yasunari Otawara and Akira Ogawa

*Stroke*. 2009;40:448-453; originally published online December 12, 2008; doi: 10.1161/STROKEAHA.108.515775

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2008 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/40/2/448

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Stroke* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Stroke* is online at:
http://stroke.ahajournals.org//subscriptions/