While the goal of carotid artery stenting (CAS) is to prevent stroke in patients with severe carotid artery stenosis, as emphasized in large randomized trials,19,33 carotid revascularization sometimes improves cognitive function.12 The cognitive function of patients with internal carotid artery (ICA) stenosis, even those who are asymptomatic, has been shown to be impaired.8,21,31 Cognitive impairment is one of the most serious problems elderly persons can face, and it stands as a social problem that is increasing along with the general aging of the population. The neurocognitive course of patients who have undergone cerebral revascularization has been the subject of many studies, and the reported effects of carotid artery stenting (CAS) on cognitive function have varied from study to study. The authors hypothesized that cognitive amelioration after CAS is associated with alteration of the default mode network (DMN) connectivity, and they investigated the correlation between functional connectivity (FC) of the DMN and post-CAS changes in cognitive function in order to find a clinical marker that can be used to predict the effect of cerebral revascularization on patients’ cognitive function in this preliminary exploratory study.

OBJECTIVE The neurocognitive course of patients who have undergone cerebral revascularization has been the subject of many studies, and the reported effects of carotid artery stenting (CAS) on cognitive function have varied from study to study. The authors hypothesized that cognitive amelioration after CAS is associated with alteration of the default mode network (DMN) connectivity, and they investigated the correlation between functional connectivity (FC) of the DMN and post-CAS changes in cognitive function in order to find a clinical marker that can be used to predict the effect of cerebral revascularization on patients’ cognitive function in this preliminary exploratory study.

METHODS The authors examined post-CAS changes in cognitive function in relation to FC in patients treated for unilateral carotid artery stenosis. Resting-state functional MRI (rs-fMRI) was performed with a 3-T scanner before and 6 months after CAS in 8 patients. Neuropsychological tests (Wechsler Adult Intelligence Scale III and Wechsler Memory Scale—Revised) were administered to each patient before and 6 months after CAS. The DMN was mapped for each patient through independent component analysis of the rs-fMR images, and the correlation between FC of the DMN and post-CAS change in cognitive function was analyzed on a voxel level. Multivariable regression analysis was performed to identify preoperative factors associated with a post-CAS change in cognitive function.

RESULTS Post-CAS cognitive function varied between patients and between categories of neuropsychological tests. Although there was no significant overall improvement in Working Memory scores after CAS, post-CAS Working Memory scores changed in negative correlation with changes in FC between the DMN and the precentral/superior frontal gyrus and between the DMN and the middle frontal gyrus. In addition, the preoperative FC between those areas correlated positively with the post-CAS improvement in working memory.

CONCLUSIONS FC between the DMN and working memory–related areas is closely associated with improvement in working memory after CAS. Preoperative analysis of FC of the DMN may be useful for predicting postoperative improvement in the working memory of patients being treated for unilateral stenosis of the extracranial internal carotid artery. Clinical trial registration no.: UMIN000020045 (www.umin.ac.jp/ctr/index.htm) https://thejns.org/doi/abs/10.3171/2018.7.JNS18404

KEYWORDS carotid artery stenting; cognitive change; working memory; default mode network; functional connectivity; vascular disorders
been the focus of many studies, and the reported effects of CAS on cognitive function have varied from study to study.¹²,²⁶,³⁷ The discrepancy is attributable to differences in several patient-related variables, e.g., age, cerebral hemodynamics, side of treatment, previous stroke, and degree of stenosis.¹⁵,¹⁸,²⁴,²⁷ Currently, it is not possible to predict the effect of CAS on cognitive function.¹²

Resting-state functional MRI (rs-fMRI) is increasingly used to examine brain connectivity, so-called functional connectivity (FC), and its relation to cognition and behavior. In particular, rs-fMRI studies have elucidated changes in the default mode network (DMN) associated with cognitive impairment in several disorders, e.g., Alzheimer’s disease, multiple sclerosis, traumatic brain injury, idiopathic normal pressure hydrocephalus, and attention deficit hyperactivity disorder.⁵,⁶,¹⁷,²⁰,²³,³² Furthermore, recent studies have pinpointed the DMN alteration involved in cognitive decline in patients with cerebral vascular disease.⁸,¹⁰

We hypothesized that post-CAS improvement in cognitive function is associated with DMN alteration and that preoperative DMN connectivity is predictive of such improvement in cognitive function. This preliminary, small-sample, prospective exploratory study was performed to investigate the correlation between a post-CAS change in cognitive function and the FC of the DMN in order to find a clinical marker that can be used to predict the effect of cerebral revascularization on patients’ cognitive function.

Methods

Study Patients

The study group comprised 8 male patients ranging in age from 59 to 78 years (mean 69.3 ± 6.2 years) and in education level from 9 to 12.5 years (mean 11.2 ± 1.4 years). These were testable patients with unilateral stenosis of the extracranial ICA who were being treated at the Osaka General Medical Center or Hanwa Memorial Hospital between August 2014 and April 2016. The patients were consecutive, except that no patient with a neurological comorbidity, severe medical disorder, or functional disability was included in the study. The degree of patients’ carotid stenosis was assessed angiographically and recorded as described in the North American Symptomatic Carotid Endarterectomy Trial (NASCET).⁵ All 8 patients were right-handed, native Japanese speakers. Seven of the patients had suffered a stroke more than 3 months before CAS and had only minor neurological sequelae; the other patient had no history of cerebral infarction.

The study was approved by the institutional review boards of Osaka General Medical Center and Hanwa Memorial Hospital, and written informed consent for participation in the study was obtained from all 8 patients included. This study was registered with the UMIN Clinical Trials Registry, and its clinical trial registration no. is UMIN000020045 (www.umin.ac.jp/ctr/index.htm).

Neuropsychological Testing

Each patient was seen by a certified, experienced neuropsychologist who used the Japanese versions of both the Wechsler Adult Intelligence Scale III (WAIS-III) ³⁴ and the Wechsler Memory Scale–Revised (WMS-R)³⁵ for evaluation. These neuropsychological tests have been standardized for the Japanese population. The WAIS-III measures general intellectual functioning and yields a performance intelligence quotient (PIQ), verbal intelligence quotient (VIQ), and full-scale intelligence quotient (FIQ), along with 4 secondary indices, namely, the Verbal Comprehension Index, Working Memory Index, Perceptual Organization Index, and Processing Speed Index. The WMS-R is used to assess general memory, verbal memory, delayed memory, visual memory, attention, and concentration. These neuropsychological tests were administered to each patient before and 6 months after CAS.

rs-fMRI

rs-fMRI imaging was performed before and 6 months after CAS at Hanwa Memorial Hospital. A 3-T scanner (Vantage Titan 3T, Toshiba Medical Systems Corp.) was used, and for the functional images, axial slices were acquired with a single-shot gradient echo-planar imaging sequence (TR 4000 msec, TE 25 msec, flip angle 90°, FOV 256 mm, voxel size 2 × 2 × 4 mm, 92 repetitions). Resting-state functional images were acquired for each patient, who was instructed to relax, stay awake, lie still, and think of nothing in particular while keeping his eyes open. The first 5 images in each run were discarded to allow magnetization to reach equilibrium. A high-resolution T1-weighted structural image (TR 400 msec, TE 16.5 msec, flip angle 90°, FOV 256 mm, isotropic voxel size 0.5 mm) was acquired during the same session.

Image Analysis

Image preprocessing was performed with SPM12 (Wellcome Centre for Human Neuroimaging; http://www.fil.ion.ucl.ac.uk/spm/software/spm12/), which was designed to aid in the analysis of functional neuroimaging data. Functional images were realigned to the first echo-planar image. Rigid body transformation described by 6 estimated parameters was applied to correct for within-run head motion. The images were then spatially normalized to a standard template (Montreal Neurological Institute [MNI]), resampled to 3-mm cubic voxels, and spatially smoothed by convolution with an isotropic Gaussian kernel (full width at half maximum = 8 mm). Structural images were segmented into individual white matter, gray matter, and cerebrospinal fluid masks. Data were bandpass filtered (0.008 Hz < f < 0.09 Hz), further processed, and corrected by means of the CONN functional connectivity toolbox (www.nitrc.org/projects/conn/). Sources of spurious variance, such as signals from white matter, cerebrospinal fluid (5 dimensions), and movement parameters extracted from the realignment process, were removed by linear regression. CONN incorporates an anatomical component-based noise correction method (aCompCor),⁴ which has been shown to effectively reduce physiological noise and noise from other sources in the blood oxygen level–dependent (BOLD) contrast signal.

To examine change in brain connectivity subsequent to CAS, we used the independent component analysis feature of CONN.³⁶ Independent component analysis is a data-driven computational method that can be used to
identify intrinsic brain networks and has been widely applied to rs-fMRI data. We used independent component analysis to extract the DMN, which is thought to be the key brain network for cognitive function. We identified DMN components using group-level independent component analysis. Group-level DMN components (both spatial maps and time courses) were then back reconstructed for each subject. The time course of the DMN represents the average pattern of coherent brain activity in the network, and the intensity of this pattern of brain activity across the voxels is expressed in the associated spatial map.

**Statistical Analysis**

Results of the WAIS-III and WMS-R tests are shown as mean ± standard deviation scores. Differences between pre- and post-CAS scores were analyzed by means of the Wilcoxon signed-rank test for paired samples. Statistical analyses were performed using JMP software (version 12.0, SAS Institute Inc.).

We then examined the correlation between change in the secondary WAIS-III indices (Verbal Comprehension, Working Memory, Perceptual Organization, and Processing Speed) and voxel-wise change in FC of the DMN. The statistical threshold was set to $p < 0.005$ uncorrected at the voxel level and $p < 0.05$ false discovery rate (FDR)-corrected at the cluster level. When a significant cluster was found, strengths of the correlation between the preoperative FC and preoperative cognitive performance and the postoperative change in cognitive performance were assessed on the basis of Pearson’s correlation coefficient.

Correlates of post-CAS improvement in cognitive function were determined by means of logistic regression modeling. Clinical variables were first evaluated for marginal association with post-CAS improvement in cognitive function (as assessed with the WAIS-III and WMS-R) by means of univariate logistic regression. Factors for which a significant ($p \leq 0.20$) marginal association was found were then entered into a single multivariate logistic regression model.

Additionally, to clarify the effect of cerebral blood flow on cognitive function, we analyzed the relation between pre-CAS NASCET% stenosis and baseline cognitive function and between post-CAS change in NASCET% stenosis (pre-CAS NASCET% stenosis minus post-CAS NASCET% stenosis) and post-CAS improvement in cognitive function.

**Results**

**CAS Procedure and Postoperative Follow-Up**

Starting 7 days before CAS, patients received oral antiplatelet drugs (aspirin 100 mg and clopidogrel 75 mg). After a local anesthetic was applied, CAS was performed with the aid of an embolic protection device and was successful in all 8 patients. Seven patients received a closed-cell stent (WALLSTENT, Boston Scientific), and 1 patient received an open-cell stent (Precise, Cordis). All 8 patients completed the 6-month WAIS-III testing, and 7 of the 8 patients completed the WMS-R testing.

The patient and clinical characteristics at the time of CAS are summarized in Table 1. CAS was performed on the left side in 6 patients and on the right side in 2. There were no significant differences in preoperative cognitive function between patients who underwent treatment on the left and those treated on the right side (Table 2). For all 8 patients, the postoperative course was uneventful, and none suffered a further cerebral ischemic event. Hyperperfusion syndrome did not develop in any patient.

<table>
<thead>
<tr>
<th>Pt Age (yrs), Sex</th>
<th>Side of Tx</th>
<th>Previous Stroke</th>
<th>Previous CAS/CEA</th>
<th>Education Level (no. of yrs)</th>
<th>Pre-CAS Stenosis</th>
<th>Post-CAS Stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>69, M 67, M 63, M 70, M 74, M 78, M 59, M 74, M</td>
<td>Rt Lt Rt Lt Lt Rt Lt Lt</td>
<td>Bilat None Lt Lt Lt Rt CAS None</td>
<td>None None None None None</td>
<td>11 12 12 9 9 12</td>
<td>51% 84% 61% 99% 50% 66% 77% 71%</td>
<td>8% 0% 6% 24% 26% 26% 5% 15%</td>
</tr>
</tbody>
</table>

*CEA = carotid endarterectomy; Pt = patient; Tx = treatment.*

<table>
<thead>
<tr>
<th>Test</th>
<th>Lt Side Treated</th>
<th>Rt Side Treated</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WAIS-III</td>
<td>93.2 ± 17.6</td>
<td>93.5 ± 23.3</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>94.7 ± 13.9</td>
<td>96.5 ± 20.5</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>89.3 ± 11.8</td>
<td>96.5 ± 14.8</td>
<td>0.62</td>
</tr>
<tr>
<td></td>
<td>101.2 ± 20.5</td>
<td>92.5 ± 13.4</td>
<td>0.74</td>
</tr>
<tr>
<td></td>
<td>93.0 ± 19.7</td>
<td>92.0 ± 22.6</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>95.2 ± 16.4</td>
<td>106.0 ± 24.0</td>
<td>0.50</td>
</tr>
<tr>
<td></td>
<td>91.3 ± 18.0</td>
<td>78.0 ± 4.2</td>
<td>0.24</td>
</tr>
<tr>
<td>WMS-R</td>
<td>53.8 ± 16.4</td>
<td>43.5 ± 36.1</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>45.8 ± 12.9</td>
<td>43.0 ± 18.4</td>
<td>0.74</td>
</tr>
<tr>
<td></td>
<td>99.0 ± 28.2</td>
<td>86.5 ± 54.4</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td>58.7 ± 14.9</td>
<td>55.0 ± 9.9</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>59.3 ± 10.8</td>
<td>51.0 ± 52.3</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Values expressed as the mean ± standard deviation, unless indicated otherwise. WAIS-III results are expressed as indices, and WMS-R results are expressed as raw scores.
Angiography performed at 6 months confirmed that no restenosis had occurred.

**Postoperative Cognitive Function**

FIQ, VIQ, and Verbal Comprehension scores for all patients increased significantly after CAS. Because the increase in scores varied widely between patients, the standard deviations of the increases in scores were larger than the mean increases in scores (Table 3).

**Correlation Between Change in Cognitive Function and Change in FC of the DMN**

From the 20 independent components computed by means of independent component analysis, we extracted the anterior part of the DMN (aDMN) and posterior part of the DMN (pDMN; Fig. 1). Analysis of the correlation between the change in FC of the pDMN at the voxel level and the increase in Working Memory scores revealed 2 suprathreshold clusters in the left frontal lobe (Fig. 2). One cluster was located in the precentral/superior frontal gyrus (SFG; MNI coordinates xyz = [-28, 10, 72], Brodmann areas 4 and 6) and comprised 241 voxels, and the other cluster was located in the middle frontal gyrus (MFG; MNI coordinates xyz = [-30, 28, 38], Brodmann area 8) and comprised 176 voxels. Two regions of interest from the suprathreshold clusters were identified for further statistical analysis. The change in FC of the clusters in the

**TABLE 3. Pre- and postoperative WAIS-III and WMS-R scores and change in scores**

<table>
<thead>
<tr>
<th>Test</th>
<th>Before CAS</th>
<th>6 Mos After CAS</th>
<th>Change</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WAIS-III</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FIQ</td>
<td>93.3 ± 17.3</td>
<td>98.6 ± 20.6</td>
<td>5.38 ± 5.90</td>
<td>0.02</td>
</tr>
<tr>
<td>VIQ</td>
<td>95.1 ± 14.1</td>
<td>101.0 ± 16.9</td>
<td>5.88 ± 5.33</td>
<td>0.02</td>
</tr>
<tr>
<td>Verbal Comprehension Index</td>
<td>91.0 ± 11.9</td>
<td>97.0 ± 15.0</td>
<td>6.13 ± 5.22</td>
<td>0.01</td>
</tr>
<tr>
<td>Working Memory Index</td>
<td>99.0 ± 18.5</td>
<td>101.0 ± 19.5</td>
<td>2.00 ± 4.81</td>
<td>0.14</td>
</tr>
<tr>
<td>PIQ</td>
<td>92.8 ± 18.8</td>
<td>96.0 ± 20.5</td>
<td>3.25 ± 6.18</td>
<td>0.09</td>
</tr>
<tr>
<td>Perceptual Organization Index</td>
<td>97.9 ± 17.3</td>
<td>101.8 ± 20.5</td>
<td>3.88 ± 7.99</td>
<td>0.11</td>
</tr>
<tr>
<td>Processing Speed Index</td>
<td>88.0 ± 16.5</td>
<td>91.5 ± 13.9</td>
<td>3.50 ± 10.5</td>
<td>0.19</td>
</tr>
<tr>
<td><strong>WMS-R</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal memory</td>
<td>53.3 ± 20.7†</td>
<td>64.6 ± 16.5†</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Visual memory</td>
<td>47.3 ± 12.4†</td>
<td>50.4 ± 14.4†</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>General memory</td>
<td>100.6 ± 32.2†</td>
<td>114.4 ± 26.0†</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Attention &amp; concentration</td>
<td>60.3 ± 12.0†</td>
<td>59.7 ± 13.8†</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Delayed recall</td>
<td>59.7 ± 22.7†</td>
<td>64.4 ± 25.5†</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

NA = not applicable.  
Boldface type indicates statistical significance.  
* Per the Wilcoxon signed-rank test.  
† Mean score for 7 of the 8 study patients.

**FIG. 1.** Anterior (left) and posterior (right) components of the DMN extracted by means of independent component analysis. Both components included the precuneus, posterior cingulate cortex, bilateral lateral occipital cortices, and medial prefrontal cortex.

**FIG. 2.** Areas in which the changes in the pDMN significantly correlated with the changes in working memory. One cluster was located in the precentral/SFG, and the other cluster was located in the MFG.
left precentral/SFG and in the MFG correlated negatively with the change in the Working Memory score ($p = 0.02$, $r = -0.78$ and $p < 0.05$, $r = -0.71$, respectively). A significant correlation was not found between change in FC of the pDMN and any other test score, and neither was there a significant correlation between change in FC of the aDMN and change in WM and preoperative FC in the precentral/SFG and MFG.

Correlation Between Preoperative FC, Preoperative Working Memory Scores, and Increases in Working Memory Scores

Preoperative FC between the pDMN and left precentral/SFG and between the pDMN and left MFG did not correlate with preoperative Working Memory scores but did correlate with postoperative increases in Working Memory scores ($r = 0.93$, $p = 0.0008$ and $r = 0.81$, $p = 0.01$, respectively; Fig. 3).

Preoperative FC of the pDMN–left precentral/SFG and of the pDMN–left MFG and age were associated at the $p \leq 0.20$ level with the postoperative increase in Working Memory scores (Table 4). When these variables were entered into a multivariate model, only the preoperative FC of the pDMN–precentral/SFG was shown to have an influence on the change in Working Memory scores. Because of the strong correlation between preoperative FC of the pDMN–MFG and preoperative FC of the pDMN–precentral/SFG ($r = 0.91$, $p < 0.01$), we excluded preoperative FC of the pDMN–MFG as a covariate in the multivariate analysis.

There was, however, no significant correlation between preoperative NASCET% stenosis and baseline Working Memory score ($p = 0.37$) and no significant correlation between change in NASCET% stenosis and improvement in Working Memory score ($p = 0.72$).

Discussion

In this preliminary exploratory study utilizing WAIS-III, WMS-R, and rs-fMRI, we examined the change in cognitive function after CAS in relation to FC of the DMN in patients with unilateral carotid artery stenosis. Improvement in cognitive function after CAS varied between patients and between the types of cognitive function tested (between subtests). Our main finding was that patients’ post-CAS working memory improved along with post-CAS decreases in FC of the pDMN–precentral/SFG and pDMN–MFG. Furthermore, preoperative FC of the pDMN–precentral/SFG and pDMN–MFG correlated positively with the post-CAS improvement in working memory.

Like other investigators, we found variations in the post-CAS improvement in cognitive function, both per patient and per type of function being tested. These variations may be attributable to the different types of neuropsychological tests used in the studies and to differences in background clinical factors, including patients’ cerebral hemodynamics.

In our patients, the post-CAS changes in FC of the...
TABLE 4. Results of univariate and multivariate analysis of 8 factors with potential influence on working memory after CAS

<table>
<thead>
<tr>
<th></th>
<th>Univariate Analyses</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preop FC of pDMN–pre–central/SFG</td>
<td>F = 39.30, p &lt; 0.01</td>
<td>F = 48.68, p &lt; 0.01</td>
</tr>
<tr>
<td>Preop FC of pDMN-MFG</td>
<td>F = 11.53, p = 0.015 Excluded</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>F = 2.18, p = 0.19</td>
<td>F = 4.69, p = 0.08</td>
</tr>
<tr>
<td>Side of Tx</td>
<td>F = 1.20, p = 0.32</td>
<td></td>
</tr>
<tr>
<td>Preop Working Memory score</td>
<td>F = 0.04, p = 0.85</td>
<td></td>
</tr>
<tr>
<td>NASCET% stenosis</td>
<td>F = 0.03, p = 0.87</td>
<td></td>
</tr>
<tr>
<td>NASCET% stenosis change</td>
<td>F = 0.14, p = 0.72</td>
<td></td>
</tr>
<tr>
<td>Education level</td>
<td>F = 0.55, p = 0.49</td>
<td></td>
</tr>
</tbody>
</table>

Boldface type indicates statistical significance.

DMN–precentral/SFG and DMN-MFG correlated inversely with post-CAS improvement in working memory. The precentral cortex, SFG, and MFG are activated during assessments that are relatively high in working memory load. The DMN appears to be activated when individuals are engaged in stimulus-independent thought, such as autobiographical memory and imagining the future, and activation of the DMN typically decreases during external or attention-demanding tasks involving mental control. Therefore, the DMN is optimally inversely correlated with brain networks commonly activated for external tasks that demand attention and mental control, regions such as the precentral cortex, SFG, and MFG. The magnitude of the inverse correlation between the DMN and the working memory network has been shown to correlate with working memory performance. In our patients in whom FC of the DMN decreased and working memory improved after CAS, DMN FC with the precentral/SFG and MFG may have returned to its normal state along with the improvement in cerebral blood flow. As far as we know, this is the first report of such restoration of FC in conjunction with intervention-based recovery of working memory.

Importantly, we found that Working Memory scores improved in significant positive correlation with preoperative FC of the pDMN–precentral/SFG and pDMN-MFG; that is, working memory improved only in the patients in whom a positive correlation between FC of the DMN and that of the working memory–related area was seen before CAS. This correlation was independent of the preoperative Working Memory score as well as the side of treatment, patient age, and NASCET% stenosis. Therefore, an inverse correlation between FC of the DMN and the precentral/SFG and MFG could be an important predictive factor for improvement in working memory after CAS.

In this study, the pre-CAS NASCET% stenosis did not correlate with patients’ baseline Working Memory scores, and the change in NASCET% stenosis did not correlate with the post-CAS improvement in Working Memory scores. The small patient group may explain why we did not find a correlation between these variables, and we assume that background factors in addition to the severity of carotid artery stenosis, factors such as collateral blood flow and peripheral arteriosclerosis, affected patients’ cognitive function.

We note several important study limitations. The first is that a power analysis was not performed to determine the precise sample size needed for testing our hypothesis. Rather, our study was conducted as a preliminary investigation in a small group of patients. The second limitation is that the size of the study might have prevented elucidation of any effect that the treatment side might have had on patients’ postoperative cognitive function. Further studies involving larger patient groups (e.g., multicenter studies) are needed to confirm our results. The third limitation is that our study did not include assessment of brain perfusion. The relation among FC, regional cerebral blood flow change, and cognitive function is very interesting, and results of brain perfusion scanning should be included in a future study. In addition, whether a learning effect played a role in the increase in patients’ test scores after carotid revascularization was not ruled out. However, more than 6 months passed between CAS and reevaluation, so a learning effect, if present, was probably minimal. Despite these limitations, we believe that our study results are impressive enough to substantiate the argument that rs-fMRI study has the potential to predict cognitive change after CAS.

In this preliminary study, we did not explore in depth the mechanism responsible for the cognitive decline or the mechanism responsible for the observed restoration of cognitive function. Longitudinal investigation of working memory that includes both preoperative and postoperative working memory and rs-fMRI assessment of FC in a large number of patients is warranted to confirm and expand upon our findings.

Conclusions

Although wide variation exists between individual patients in the degree to which cognitive function improves after CAS, FC between the DMN and the working memory–related area correlates closely with the improvement in working memory function after CAS. Preoperative FC of the DMN could prove useful for the prediction of postoperative improvement in working memory.

Acknowledgments

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References

5. Bonnelle V, Leech R, Kinunnen KM, Ham TE, Beckmann...


Disclosures
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Author Contributions
Conception and design: Tani. Acquisition of data: Tani, Yaegaki, Nishino, Fujimoto, Hashimoto, Horiiuchi, Nishiguchi. Analysis and interpretation of data: Tani, Yaegaki. Drafting the article: Tani. Critically revising the article: Kishima. Reviewed submitted version of manuscript: Yaegaki, Nishino, Fujimoto, Hashimoto, Horiiuchi, Nishiguchi, Kishima. Administrative/technical/material support: Nishino. Study supervision: Kishima.

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