fMRI Demonstrates Diaschisis in the Extrastriate Visual Cortex

Amy Brodtmann, MBBS, FRACP, PhD; Aina Puce, PhD; David Darby, MBBS, FRACP, PhD; Geoffrey Donnan, MBBS, FRACP, MD

Background and Purpose—Diaschisis may play a critical role in motor recovery, but in other cortical networks its role is unclear. Some visual system regions, such as the fusiform gyri, depend on intact striate regulation for their function. We evaluated visual cortical diaschisis by serial functional magnetic resonance imaging.

Methods—Using a high-level visual activation task, we studied patients with visual system stroke by functional magnetic resonance imaging within 10 days and at 6 months. Their activation data were compared with those of age-appropriate healthy control subjects.

Results—Three patients were studied. In the short term, patients displayed absent or significantly reduced activation in ventral extrastriate sites. All displayed a restitution of activation to these sites at 6 months.

Conclusions—Functional magnetic resonance imaging revealed evidence of ipsilesional cortical diaschisis within ventral extrastriate sites. Diaschisis may play an underrecognized role in visual recovery after stroke. (Stroke. 2007;38:2360-2363.)

Key Words: diaschisis ■ functional magnetic resonance imaging ■ stroke

The term “diaschisis” refers to depressed metabolic function of the cortex anatomically distant from but functionally connected to a focal brain lesion.1,2 Baron and coworkers1 initially used positron emission tomography to demonstrate crossed cerebellar diaschisis, and it has been incidentally documented in motor functional magnetic resonance imaging (fMRI) studies.3 Diaschisis is believed to contribute to poststroke plasticity,3,4 but its contribution to visual recovery is unclear.5,6

fMRI is a novel imaging modality for diaschisis detection that allows visualization of blood flow changes at high resolution. Blood oxygen level–dependent signal changes are a sensitive downstream measure of neuronal activation.7 The return of blood oxygen level–dependent activation in the extant anatomically connected cortex is interpreted here as evidence of diaschisis.

We postulated that visual system diaschisis could be documented by serial fMRI. We studied stroke patients within 10 days and at 6 months. We predicted diaschisis particularly in the fusiform and lingual gyri, regions known to have greater dependence on striate function.8 Naturalistic stimuli were used to target ventral activation.9 Visual recovery was not correlated with diaschisis owing to small study numbers.

Subjects and Methods
Informed, written consent was obtained. The study was approved by the Austin Health ethics committee.

Participants
Control Subjects
Study criteria have been described in detail elsewhere.9 Healthy age- and sex-matched control subjects had normal corrected vision. Control subjects were carefully screened for prior vascular events.

Patient Inclusion and Exclusion Criteria
Stroke patients were included with a confirmed first-ever acute ischemic infarct with corresponding perimetric defect. Usual MRI exclusion criteria applied. Neuropsychological screening was performed as required.

Experimental Design
Stroke patients were recruited from the Austin Health Stroke Unit and received standard stroke management, including admission diffusion- and perfusion-weighted MRI scans. Patients were studied within 10 days of their stroke (session 1) and at 6 months (session 2), with automated visual perimetry at both sessions. Control subjects had identical testing during 2 sessions 6 months apart.

Visual Field Testing
Visual fields were assessed with the Medmont M600 automated perimetry neurologic field program, including fixation loss errors (Medmont, Camberwell, Victoria, Australia). Fixation loss errors were compared between groups by Student’s t test.

Magnetic Resonance Imaging
Data acquisition has been described in detail elsewhere.9 Images were acquired on a 3-T GE Horizon LX MRI scanner (GE Systems, Milwaukee, Wis): structural whole-brain axial 3-dimensional spoiled gradient recalled echo and coronal T1 images and functional coronal half-brain gradient-echo echoplanar images (14 posterior slices).9

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We used a block-design activation task with alternating central presentations of gray-scale unfamiliar faces (FACE), scrambled faces (SCRF), and a 50% gray field with a central black fixation cross (GRAY) in a repeated FACE, GRAY, SCRF, GRAY sequence. Eye movements were not monitored in the scanner. Subjects kept their eyes directed on the fixation cross and detected a random central white cross target, raising their left thumb on target detection. Subjects were observed for target detection accuracy. Error rates were compared by Student’s t test. MEDx 3.3 (Sensor Systems Inc, Sterling, Va) was used for data analysis. Test maps were obtained for each comparison of interest, e.g., FACE versus GRAY. Only FACE data are presented here, because these stimuli produced more ventral extrastriate activation in healthy control subjects. t test maps were thresholded to a probability value $<$0.001, uncorrected. Activated voxel counts (AVCs) were calculated for anatomic regions of interest. Data were not normalized or smoothed, remaining in native space to allow for stroke-related variability.

Results

Control Subject Characteristics
Twenty-four healthy control subjects age 33 to 89 years (mean±SE age, 65.7±3.6 years) were studied, 6 from each of the fourth, seventh, eighth, and ninth decades; 9 women, 4 left-handed subjects9 (Figure 1). Eight subjects, 2 from each decade, were randomly chosen for repeat analysis (4 women; mean±SE age, 64.3±6.8 years).

Stroke Patient Characteristics
Three patients (2 men) were studied, with an age range of 32 to 85 years (mean±SE age, 55.3±15.6 years), 2 with a right posterior cerebral artery stroke (both cardioembolic) and 1 with a right anterior middle cerebral artery stroke (carotid dissection). Admission diffusion- and perfusion-weighted imaging revealed no evidence of penumbra. Mean time to fMRI study was 7.3±1.5 days (range, 5 to 10 days).

Automated Perimetric Findings
Visual fields for all control subjects were normal. Mean fixation error rates and ranges were comparable for sessions 1 and 2: 5.6±1.8 (range, 1 to 16) and 5.3±1.7 (range, 1 to 13), respectively. Patients demonstrated hemianopic visual loss corresponding to their stroke site. A variable amount of recovery was seen (Figure 2). Mean fixation error rates and ranges did not significantly differ between sessions 1 and 2: 9.0±4.7 (range, 2 to 18) and 13.3±9.5 (range, 1 to 32), respectively. There was no significant difference between patient and control error rates for either session.

Target Detection Accuracy
All participants detected targets with a high degree of accuracy. There were no significant differences in target detection between controls (97.8±3.8% for both sessions) and patients (accuracy of 97.2±2.8% for both sessions).

fMRI Activation Patterns

Control Subjects
Robust fusiform activation was seen in all subjects9 (Figure 1). Importantly, regional activated voxel counts were not significantly different between sessions (Table).

Stroke Patients

Short-Term Study
Patients demonstrated absent or significantly reduced ipsilesional ventral extrastriate activation (see the Table and Figure.
including the patient with anterior middle cerebral artery infarction (P3). Contralesional activation patterns were comparable with those of controls (Table and Figures 1 and 2).

**Long-Term Study**

Ipsilesional fusiform activated voxel counts normalized over time; P3 demonstrated the most profound return of fusiform activation (Figure 2). Contralesional ventral extrastriate activated voxel counts were significantly less than in controls (Table).

**Discussion**

We documented blood oxygen level–dependent restitution in ventral extrastriate areas, interpreted here as evidence of diaschisis. This ipsilesional fusiform diaschisis was found in

<table>
<thead>
<tr>
<th>Activated Voxel Counts for Patients and Control Subjects</th>
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<tr>
<td>Site</td>
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<td>Session 1</td>
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<td>IVES</td>
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Activated voxel counts for ipsilesional (I) and contralesional (C) ventral extrastriate (VES) and striate cortices (STR) for patients and controls.

Significant differences at *P<0.01, †P<0.001.
both striate infarction and striate cortical deafferentation (P3). The latter highlights the importance of preserved striate and corticocortical connections for ventral extrastriate function. Attentional fluctuations would not explain these findings, because measures of vigilance were comparable for each session. The areas were too remote from the responsible arterial occlusions to be significantly affected by decreased perfusion and edema, and short-term fMRI was performed when resolution of the ischemic penumbra is usual.

Conclusions
Our data provide fMRI evidence of ipsilesional ventral extrastriate cortical diaschisis in patients with visual pathway stroke. Our findings illustrate the dependence of normal ventral extrastriate activity on intact striate function. However, our study numbers were too small to correlate diaschisis with visual function, but its role in visual recovery is worthy of further fMRI investigation.

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Disclosures
None.

References
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