Brain Stem Infarction and Diaschisis
A SPECT Cerebral Perfusion Study

F. Fazekas, MD; F. Payer, MD; H. Valetitsch, MD; R. Schmidt, MD; E. Flooh, PhD

Background and Purpose: We studied six patients suffering from pure, unilateral brain stem infarction to explore the association of remote cerebral and cerebellar blood flow changes with damage at different sites of this region of the brain.

Methods: We used single-photon emission computed tomography and \(^{123}\)I iodoamphetamine to measure regional differences in tracer uptake. Qualitative image analysis and calculated asymmetry indexes were correlated to the location of the infarcted area on magnetic resonance imaging and to the patients` clinical findings.

Results: Significant perfusion asymmetries were noted in the two patients with infarction in the upper pons but not in those with lesions below this level. They comprised a contralateral cerebellar and ipsilateral supratentorial hypoactivity that was most marked in the frontoparietal cortex. There was no clear relation between the patterns of cerebral or cerebellar tracer uptake and specific neurological findings.

Conclusions: Remote perfusion changes after pure brain stem infarction may be seen both infratentorially and supratentorially and depend on the lesion site rather than on the neurological deficit. In this context, our study confirmed damage to the corticopontocerebellar pathways as the key event in the genesis of a crossed cerebellar diaschisis. The exact mechanisms causing ipsilateral cerebral hemispheric diaschisis await further clarification. (Stroke 1993;24:1162-1166)

Key Words • brain stem • cerebral blood flow • diaschisis • tomodraphy, emission computed

Contralateral hyperperfusion of the cerebellum may be seen in up to 50% of patients with hemispheric stroke.\(^1\)\(^-\)\(^3\) It occurs preferentially with large infarcts and damage to the frontoparietal lobes.\(^4\) A similar phenomenon can be observed in the opposite direction; ie, contralateral cerebral hemispheric blood flow was shown to be significantly depressed in patients with unilateral cerebellar hematomas or infarcts.\(^5\)\(^-\)\(^7\) Remote deactivation from damage to the fiber tracts of the cerebrocerebellar loop is thought to be the most likely explanation for both types of diaschisis.\(^8\)\(^-\)\(^7\)

This hypothesis may gain further support from cerebral blood flow studies in patients with lesions of the brain stem because these pathways traverse parts of that area. However, single-case studies came up with conflicting results. There have been two reports of patients with pontine infarction and a crossed cerebellar hypoperfusion\(^8\)\(^-\)\(^9\); however, such a lesion was associated with ipsilateral hypoactivity in another patient.\(^10\) We therefore describe the single-photon emission computed tomography (SPECT) perfusion patterns observed in a selected group of patients with unilateral brain stem infarction and relate these findings to lesion topography and the patients` neurological deficits.

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TABLE 1. Demographic Data and Clinical and Imaging Findings

<table>
<thead>
<tr>
<th>Patient/age/sex</th>
<th>Neurological findings</th>
<th>Imaging findings</th>
<th>SPECT</th>
<th>Study interval*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/62/F</td>
<td>Left mild-to-moderate hemiparesis</td>
<td>Right upper pontine basis and tegmentum infarct</td>
<td>Left cerebellar and right frontoparietal hypoactivity</td>
<td>6 Days</td>
</tr>
<tr>
<td>2/72/F</td>
<td>Severe left hemiparesis and hemihypertension, dysarthria, vertigo</td>
<td>Right central upper pontine infarct extending into midpontine basis and tegmentum, bilateral small patchy WMH</td>
<td>Left cerebellar and right frontoparietal hypoactivity</td>
<td>1 Day</td>
</tr>
<tr>
<td>3/69/F</td>
<td>Mild right hemiparesis and ataxia, dysarthria, vertigo</td>
<td>Left midpontine basis and tegmentum infarct, two minute lacunes in left lenticular nucleus and thalamus, bilateral small patchy WMH</td>
<td>Normal</td>
<td>1 Day</td>
</tr>
<tr>
<td>4/54/M</td>
<td>Mild right hemiparesis, dysarthria, vertigo</td>
<td>Left midpontine basis and tegmentum infarct</td>
<td>Normal</td>
<td>1 Day</td>
</tr>
<tr>
<td>5/66/M</td>
<td>Right hemiataxia, decreased sensation left body, right Horner’s syndrome, hoarseness, dysphagia, vertigo</td>
<td>Right dorsolateral medulla infarct</td>
<td>Normal</td>
<td>30 Days</td>
</tr>
<tr>
<td>6/56/M</td>
<td>Left hemiataxia, decreased sensation on left side of face, left Horner’s syndrome, hoarseness, dysphagia, nystagmus</td>
<td>Left dorsolateral medulla infarct, bilateral punctate WMH</td>
<td>Normal</td>
<td>1 Day</td>
</tr>
</tbody>
</table>

MRI, magnetic resonance imaging; SPECT, single-photon emission computed tomography; WMH, white matter hyperintensities.

*Interval between onset of neurological symptoms and SPECT study.

Order of each cerebellar hemisphere, to detect tracer asymmetries outside this rectangle, a second ROI was drawn around the contours of one entire cerebellar hemisphere and then mirrored onto the other hemisphere, with the midline serving as axis. In case of visual asymmetry, the size of this ROI was derived from the smaller half of the cerebellum to keep the probability of false-positive side-to-side differences at a minimum. The asymmetry index was considered to be abnormal if it was outside the 95% confidence interval of values collected from a group of 10 asymptomatic age-comparable volunteers (age range, 44 to 66 [mean, 56] years) studied during the same time period. The confidence limits were determined by using the two-tailed t test value corresponding to \( P < .05 \) at nine degrees of freedom.

We performed MRI studies on all patients and control subjects with a 1.5-T magnet (Gyroscan S15, Philips, Eindhoven, The Netherlands) by using conventional spin-echo techniques (repetition time/echo time [TR/TE], 2400 to 2800/30, 90 msec and TR/TE, 600/30 msec) in the transverse and sagittal orientations, with a slice thickness of 5 mm. In addition, all patients underwent routine extracranial and transcranial Doppler sonography (Vingmed CFM 750, Diasonics, Horten, Norway, and Transcran, EME, Ueberlingen, FRG). A review of the patients’ charts served to classify the stroke mechanisms involved according to a recent suggestion by the TOAST investigators.

**Results**

A detailed description of the patients’ neurological and MRI findings is provided in Table 1. Patients are listed according to the level of infarct in craniocaudal order. Briefly, two patients had infarcts involving the upper pons. Infarction to the midpons and medulla was noted in two subjects each. The cerebellum appeared normal in all cases. At supratentorial levels we found subtle bilateral white matter hyperintensities in five patients. Two individuals showed basal ganglia and thalamic lacunes that did not exceed a diameter of 1 to 2 mm. Bilateral white matter hyperintensities were also seen in four control subjects. Patients 1, 2, and 3 probably suffered from small-artery occlusion, cardioembolism had to be assumed in patient 5, and the cause of stroke remained undetermined in patients 4 and 6.

In the two patients with upper pontine stroke, SPECT studies yielded an abnormal perfusion pattern characterized by a relative reduction of tracer uptake in the ipsilateral hemispheric cortex and the contralateral cerebellum. Supratentorial changes were most marked in the frontoparietal lobes (Table 1 and Figure). The corresponding asymmetry indexes are shown in Table 2. No perfusion asymmetry occurred in patients with more caudally located infarcts. Doppler sonographic studies showed no hemodynamically significant stenosis of the extracranial or intracranial cerebral arteries in any of the patients examined.

The neurological examinations of patients with asymmetric cerebellar tracer uptake were unremarkable for cerebellar signs. Testing was limited, however, because they all suffered from marked motor deficits. Hemiataxia in patients with lesions located in the midpons and below was not associated with a cerebellar perfusion asymmetry. In the presence of diachisis, patients tended to have more severe motor deficits than those with a symmetric perfusion pattern (Table 1).
Acute onset of left motor hemiparesis is demonstrated in patient 1. (Patient's right side appears on reader's right.) Magnetic resonance imaging (left) reveals infarction of upper right basis pontis and tegmentum. Corresponding single-photon emission computed tomographic images (right) show diffuse hypoactivity of right frontoparietal cortex and contralateral left cerebellar hemisphere.

Discussion

We observed significant cerebellar perfusion asymmetries exclusively in patients with upper pontine stroke; these asymmetries were characterized by a lower tracer uptake contralateral to the ischemic lesion. In our sample of brain stem infarcts this was the location with the highest probability of causing damage to a significant number of descending cerebrocerebellar fiber tracts, as all still course together at that level.\(^{15,16}\) Accordingly, the patient with brain stem stroke and contralateral cerebellar hypoperfusion described by Sakai et al\(^9\) also suffered from infarction to the upper basis pontis.

The effect of midpontine lesions on the cerebellum appears to be variable. Although cerebellar blood flow was symmetrical in our two patients with infarcts at that location, Perani et al\(^9\) observed contralateral and Bowler and Wade\(^10\) ipsilateral cerebellar hypoactivity in one case each. Finally, Heiss et al\(^17\) described marginally reduced glucose consumption of both cerebellar hemispheres in another case of midpontine infarction. Such "bilateral" cerebellar diaschisis might have gone undetected by a semiquantitative analysis like ours, which relied primarily on asymmetries of tracer uptake. This inconsistency of findings may stem from differences in the involvement of the bilateral corticopontocerebellar tracts that contain the vast majority of cerebrocerebel-

<table>
<thead>
<tr>
<th>Patient</th>
<th>Lesion site</th>
<th>Cerebellum (ROI inscribed)</th>
<th>Cerebellum (ROI contour)</th>
<th>Frontal</th>
<th>Parietal</th>
<th>Occipital</th>
<th>Temporal</th>
<th>Cerebral hemisphere</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R upper pons</td>
<td>9.06*</td>
<td>8.74*</td>
<td>-2.77*</td>
<td>-4.53*</td>
<td>-3.07*</td>
<td>-0.95</td>
<td>-2.81*</td>
</tr>
<tr>
<td>2</td>
<td>R upper pons</td>
<td>8.69*</td>
<td>7.44*</td>
<td>-1.78</td>
<td>-5.36*</td>
<td>-0.92</td>
<td>1.34</td>
<td>-1.66</td>
</tr>
<tr>
<td>3</td>
<td>L middle pons</td>
<td>-0.69</td>
<td>-1.60</td>
<td>0.60</td>
<td>3.26</td>
<td>-0.01</td>
<td>0.29</td>
<td>0.91</td>
</tr>
<tr>
<td>4</td>
<td>L middle pons</td>
<td>-0.33</td>
<td>-0.20</td>
<td>1.59</td>
<td>1.93</td>
<td>-1.41</td>
<td>-1.03</td>
<td>0.44</td>
</tr>
<tr>
<td>5</td>
<td>R medulla</td>
<td>-0.46</td>
<td>0.96</td>
<td>2.43</td>
<td>0.00</td>
<td>0.32</td>
<td>3.53</td>
<td>0.00</td>
</tr>
<tr>
<td>6</td>
<td>L medulla</td>
<td>2.53</td>
<td>1.92</td>
<td>0.80</td>
<td>1.23</td>
<td>1.57</td>
<td>2.43</td>
<td>1.37</td>
</tr>
</tbody>
</table>

95% confidence interval:

-4.60 to +6.40

Asymmetry index: \((R - L)/(R + L)/2\)×100%, where R and L represent right and left count rates from corresponding regions of interest (ROIs).

*Significant asymmetry at \(P<.05\).
lar connections. As these tracts cross at midpontine level, a unilateral lesion may cause simultaneous but diverse damage to pathways projecting to both cerebellar hemispheres. Differences in sensitivity for displaying the extent of morphological damage between studies using cranial computed tomography or MRI and additional hemodynamic compromise, which we excluded in our study, may also have had some impact on the above results.

Unilateral cerebellar hypoactivity was not seen in patients with dorsolateral medullary infarction. Lesions at that site of the brain stem will damage only those fibers of the cerebrocerebellar pathways that reach the cerebellum through the inferior olive.15,16 This is a relatively small portion. Obviously, compromise of afferents from the spinal cord was insufficient to cause a detectable cerebellar diaschisis.

The association of brain stem infarction with ipsilateral cerebrocerebellar diaschisis was a finding that has not been reported previously. It occurred in the two patients with upper pontine stroke and contralateral cerebellar hypoactivity and involved preferentially the frontoparietal cortex. Various potential mechanisms deserve discussion. Reports on cerebral hemispheric diaschisis contralateral to a cerebellar hemorrhage or infarction suggest interruption of the ascending cerebellothalamicocortical projections as a potential cause.5,6 Accordingly, ischemia in our patients may have reached far enough cranially to damage these pathways after decussation of the brachium conjunctivum. The frontoparietal distribution of cerebral hemispheric hypoactivity noted in our patients would fit with the anatomic data on the projection of these tracts.18 However, such an infract extension could not be substantiated on MRI and would rarely have spared the area caudal to the decussation, which contains the uncrossed portion of analogous projections to the contralateral cerebral hemisphere.

The simultaneous presence of a crossed cerebellar and ipsilateral cerebral hemispheric diaschisis could be explained by disruption of just the corticopontocerebellar tract as well, if this would have induced both anterograde and retrograde effects. Yet a positron emission tomography study on capsular and thalamic strokes suggests that the thalamocortical projections must sustain damage before hypometabolism of the overlying cortical mantle develops.19 The authors of the same study speculate that cortical hypoactivity per se might suffice to cause a contralateral cerebellar diaschisis. The inverse could have been observed by us; i.e., cerebellar deactivation after upper pontine stroke may have back-projected to cortical areas through intact cerebellocerebral connections.

Numerous other tracts passing through or originating in the pontine tegmentum could have been also relevant to our findings. Evidence from animal studies suggests that lesions to specific brain stem nuclei such as the locus coeruleus can be associated with metabolic depression of the ipsilateral cerebral cortex, and damage to fibers of the ascending reticular activating system can alter forebrain function.4 Finally, Botet et al5 incriminated a dopaminergic pathway that originates from the dentate nucleus as a contributor to cerebellocerebral diaschisis in their patients with infarction or degenerative disorders of the cerebellum.

We found no clear association between SPECT perfusion patterns and clinical signs and symptoms. Patients with upper pontine stroke showed a contralateral hypoperfusion of the cerebellum without corresponding neurological signs, whereas ataxia was a prominent finding in three of four patients with more caudally located infarcts and symmetrical cerebellar blood flow. Such incongruity of findings is not unexpected, as ataxia may have several underlying mechanisms in addition to cerebellar dysfunction. Still, it challenges the speculation of Sakai et al,8 who concluded from the presence of a contralateral cerebellar hypoactivity in a patient with pontine stroke and ataxic hemiparesis that cerebral blood flow studies might serve to document the functional correlate of this syndrome. From our observations, the abnormalities need not have been related. Accordingly, patients with cerebellar diaschisis from supratentorial lesions rarely display cerebellar signs,4 and the results of positron emission tomography studies on cerebellar activity in ataxic hemiparesis are controversial.19,20 Except for a trend toward more severe motor impairment in patients with diaschisis, cerebral blood flow patterns of our patients were also not associated with specific sensory or motor deficits. Thus, SPECT perfusion studies in patients with brain stem infarction may not reveal findings of gross clinical significance but appear to be an excellent means of extending our concepts of diaschisis.

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