Crossed Hemispheric Diaschisis in Unilateral Cerebellar Lesions

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Background and Purpose: We studied 12 patients with unilateral cerebellar hemorrhage to look at its effect on regional cerebral blood flow.

Methods: We used single-photon emission computed tomography by continuous inhalation of xenon-133. The blood flow was quantified in the cerebellum and in nine areas of interest on the slice passing through the basal ganglia.

Results: The comparison of the blood flow values of the patients and control subjects showed a significant reduction in the contralateral hemisphere of the patients, predominantly in the frontal region and in the lenticular nucleus of the contralateral hemisphere but also in the anterointernal frontal area of the ipsilateral hemisphere. The analysis of the asymmetry indexes revealed in the same way significant differences between patients and control subjects in the frontal cortex and in the lenticular nucleus.

Conclusions: These results provided concordant evidence suggesting a blood flow reduction in the contralateral hemisphere. This phenomenon of “crossed hemispheric diaschisis” is probably related to the interruption of cerebellocortical tracts. (Stroke 1992;23:511–514)

Key Words • cerebellum • cerebral blood flow • cerebrovascular diseases • diaschisis

A reduction in metabolic activity and blood flow in the cerebellum contralateral to lesions of one cerebral hemisphere was first demonstrated by Baron et al. Since that time, other studies have confirmed this phenomenon, which has also been observed in a limited number of frontal, thalamic, or putaminal lesions. The work of Martin and Raichle has suggested effects on the ipsilateral cerebellum.

We studied the regional cerebral blood flow (rCBF) of 12 patients with cerebellar lesions to determine whether there are changes in the rCBF of the cerebral hemispheres and, more particularly, in the contralateral one.

Subjects and Methods

We examined 12 consecutive patients who had experienced a cerebellar hemorrhage without any effects on the brain stem. There were nine men and three women ranging in age from 40 to 76 (median 65) years of age. The lesion revealed by computed tomographic (CT) scan was lobar and unilateral in seven cases (left in three cases, right in four) and lobar and vermian in five cases (left in two cases, right in three). Two patients had undergone surgery to evacuate the hematoma.

We conducted the cerebral blood flow (CBF) studies 13–79 (median 26.5) days after the hemorrhage. At that time, level of consciousness was normal in all patients, and examination revealed a classic cerebellar syndrome. The degree of ataxia of the upper limb was assessed on a scale of 0 (absent) to 4 (major, absence of functional use); the same procedure was adopted for ataxia of the trunk. The total cerebellar score was the sum of the previous two scores.

The CBF was analyzed using single-photon emission computed tomography, by continuous inhalation of xenon-133, with an apparatus of the Tomomatic 64 type (Medimatic, Copenhagen). The examination was conducted under standard conditions after a 15-minute adaptation period, in dim light and silence. The ears were not plugged, but the eyes were closed. This examination lasted 4.5 minutes. The partial alveolar pressure for CO₂ (Paco₂) was recorded with a Beckman LB2 capnograph.

The measurements were obtained from three 2-cm-thick scanner slices of brain tissue from 1, 5, and 9 cm above the orbitomeatal (OM) plane (i.e., OM+1+5+9 cm). The full-width half-maximum was 12 mm and the pixel 25 mm². The reproducibility of the method has been previously described.

Blood flow values were quantified in the cerebellum on the lower slice and in nine areas (size: 650–800 mm²; 25 pixels at least) traced manually on each cerebral hemisphere on the intermediate slice (Figure 1) passing through the basal ganglia: frontal anterointernal, anteroexternal, and posteroexternal; temporal anterior and posterior; temporop-occipital; internal occipital; lenticular; and thalamic. The mean hemisphere CBF was the average of the local values. As previously described, we later calculated the cerebellar asymmetry indexes [AI%=(healthy side rCBF−lesion side rCBF)×100/(healthy side rCBF+lesion side rCBF)/2], and then the asymmetry indexes of the hemisphere areas [AI%=(lesion side rCBF−healthy side rCBF)×100/(lesion side rCBF+healthy side rCBF)/2].

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The rCBF values and then the asymmetry index values were compared with those of 24 control subjects, 14 men and 10 women, ranging in age from 21 to 73 years. For each patient, two controls were matched in terms of side of the cerebellar lesion and age. In this way, the “lesion” side at the level of the cerebellum and cerebral hemispheres was left in 10 control subjects and right in 14 others. To ensure correct matching for age, we corrected the CBF values for the control subjects, taking into account the regression lines of rCBF versus age for each area.

The Paco2 was not statistically different in patients (median 4.9%) and control subjects (5.2%), and we did not correct rCBF values for this factor. Systolic arterial blood pressure was significantly higher in the patients group than in the control group (145 versus 130 mm Hg), but we did not correct rCBF values for this other factor because, in the control group, blood pressure was highly correlated with age (r=0.558) but not with rCBF.

For statistical analysis of the rCBF and AI variations, we used repeated-measures analysis of variance (ANOVA) with an alpha risk of p<0.05 and Bonferroni corrections for multiple post hoc analysis (SAS package; SAS Institute, Cary, N.C.).

In addition to the quantitative analysis, we carried out a qualitative, visual analysis of the cartographic images (without knowing the side of the cerebellar lesion on the computed tomographic scan) to look for asymmetry in the cerebellum, anterior cortex, posterior cortex, and thalamus.

Subsequently, we looked for correlations between rCBF in each area, time after stroke (days), and the clinical cerebellar score, using the same corrections as for multiple comparisons.

Results

In our visual analysis of the cerebellum, we observed marked asymmetry with a reduction in rCBF on the lesioned side in 11 of 12 cases. Asymmetry, with an rCBF reduction on the side contralateral to the cerebellar lesion, was very often found in the anterior cortex (10 of 12 cases) (Figure 2) but was rare in the posterior cortex (four cases) and thalamus (five cases). A mild reverse asymmetry was sometimes discovered in the posterior cortex (three cases) and thalamus (two cases). In the latter area, the phenomenon was marked in one patient, in relation to a paradoxical rCBF elevation and a “dissociation” from the cortical CBF.

Table 1 shows CBF values for patients and control subjects. In the cerebellum ipsilateral to the hemorrhage, the mean CBF was lower than that of the control subjects (40.6 versus 50.5 ml/100 g/min). In the contralateral cerebellum, mean values were very close. The repeated-measures ANOVA analyzing the cerebellar CBF variations with one between-subjects factor (group, patients versus controls) and one within-subjects factor (side, lesion versus healthy) found a significant side effect (F=52.8, df=1, p=0.0001) and a significant group×side interaction (F=45.0, df=1, p=0.0001). The post hoc analysis showed that CBF values were significantly lower on the lesion side in the patient group.

On the hemisphere ipsilateral to the cerebellar lesion (lesion side), the mean CBF values were generally lower than those of the control subjects but the differences were small, with the exception of the anterointernal frontal area. In the cerebral hemisphere contralateral to the lesion (healthy side), the mean rCBF values were lower in the patients than in controls for each area of interest. A repeated-measures ANOVA analyzed the variations of the hemisphere rCBF values with one between-subjects factor (group, patients versus controls) and two within-subjects factors (side, lesion versus healthy; and area, frontal anterointernal to thalamic).

We found a significant main effect for the side (F=11.02, df=1, p=0.002) and for the area (F=45.7, df=8, p=0.0001) and a strong tendency for the group (F=4.06, df=1, p=0.051); the CBF values were lower on the healthy side. The following interactions were also significant: group×side (F=11.9, df=1, p=0.001), group×area (F=2.04, df=8, p=0.042), and group×side×area (F=2.4, df=8, p=0.018). Post hoc analysis using Bonferroni correction (p<0.05) showed that the differences between patients and control subjects were significant for the frontal anterointernal, frontal anteroexternal, frontal posteroexternal, temporo-occipital, thalamic, and lenticular areas on the healthy side and on the frontal anterointernal area on the lesion side.

In addition, in the majority of cases, the CBF reduction on the healthy hemispheric side was “harmonious.” This was shown by the highly significant coefficients of correlation between the CBF values on the frontal and temporal cortex and on the lenticular nucleus (frontal anteroexternal 0.789, p=0.0023; frontal posteroexternal 0.896, p=0.0001; temporal anterior 0.940, p=0.0001; temporal posterior 0.867, p=0.0003; and temporo-occipital 0.801, p=0.0018). The same coefficients between cortex and thalamus were lower (frontal anteroexternal 0.612, p=0.034; frontal posteroexternal 0.718, p=0.008; temporal anterior 0.818, p=0.001; temporal posterior 0.732, p=0.007; and temporo-occipital 0.712, p=0.009)
which was probably the consequence of the "dissociation" observed in some patients.

The mean cerebellar Al index of the patients (29.5%) was significantly higher \((p=4.1\times10^{-4})\) than that of the control subjects (1.3%). In the cerebral hemispheres, the mean asymmetry indexes of the patients were positive (frontal anterointernal 2.1%; frontal anteroexternal 9.1%; frontal posteroexternal 10.4%; temporal anterior 7.1%; temporal posterior 8.9%; temporoparietal 0.7%; internal occipital 1.6%; lenticular 9.9%; and thalamic 4.2%). A repeated-measures ANOVA analyzed the variations of AI, with one between-subjects factor (group, patients versus controls) and one within-subjects factor (site, frontal anterointernal to thalamic). There was a significant group effect \((F=16.01; \text{df}=1; p=0.0003)\), with AI being more elevated in patients, and a significant group x site interaction \((F=2.38; \text{df}=8; p=0.017)\); post hoc analysis showed that AI was significantly higher for patients in the anteroexternal frontal area, the posteroexternal frontal area, and the lenticular area.

Time after stroke and the cerebellar clinical score were not correlated with rCBF.

Discussion

These results, obtained in 12 patients, provided concordant evidence suggesting a reduction in the CBF for the hemisphere contralateral to a unilateral cerebellar lesion. This phenomenon has been suggested in a previous case report, but in that case the cerebellar infarction was associated with a brain stem lesion that could have caused its occurrence.

It was the reverse of the crossed cerebellar diaschisis described by Baron et al and subsequently encountered by many other authors. Interruption of the corticopontocerebellar tracts was, indeed, proposed as an explanation of this remote effect. Nonetheless, the fact that reduced cerebellar metabolism or low flow can be found in strictly thalamic lesions suggested that a retrograde mechanism or cortical hypometabolism may also play a part.

The reduction in hemispheric CBF that we observed had a number of particular features that should be emphasized. It especially involved the frontal regions of the cortex and the deeper lenticular area; the distribution was the same in the case previously described. It was also more discrete than the reduction of cortical CBF associated with thalamic or capsulolenticular lesions. This contralateral effect may be related to the essential anatomic connections between the cerebellum and the hemispheric structures. The cerebellar nuclei are the origin of efferent tracts that pass through the upper cerebellar peduncle and mesencephalic tegmentum and end on the ventrolateral and anterior ventral

Table 1. Mean (ml/100 g/min) and Standard Deviation Values of the rCBF

<table>
<thead>
<tr>
<th>Lesion side</th>
<th>Patients</th>
<th>Controls</th>
<th>Healthy side</th>
<th>Patients</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>40.6</td>
<td>6.0</td>
<td>50.5</td>
<td>8.6</td>
<td>55.3</td>
</tr>
<tr>
<td>Frontal anterointernal</td>
<td>53.2</td>
<td>11.5</td>
<td>62.1</td>
<td>10.0</td>
<td>52.7</td>
</tr>
<tr>
<td>Frontal anteroexternal</td>
<td>46.7</td>
<td>10.5</td>
<td>49.1</td>
<td>7.2</td>
<td>42.4</td>
</tr>
<tr>
<td>Frontal posteroexternal</td>
<td>51.6</td>
<td>10.9</td>
<td>53.2</td>
<td>9.1</td>
<td>46.5</td>
</tr>
<tr>
<td>Temporal anterior</td>
<td>51.1</td>
<td>9.5</td>
<td>54.3</td>
<td>8.8</td>
<td>47.7</td>
</tr>
<tr>
<td>Temporal posterior</td>
<td>52.9</td>
<td>10.9</td>
<td>56.7</td>
<td>9.6</td>
<td>49.0</td>
</tr>
<tr>
<td>Temporo-occipital</td>
<td>39.8</td>
<td>9.1</td>
<td>44.4</td>
<td>6.5</td>
<td>39.5</td>
</tr>
<tr>
<td>Internal occipital</td>
<td>51.7</td>
<td>12.2</td>
<td>56.4</td>
<td>9.5</td>
<td>52.7</td>
</tr>
<tr>
<td>Lenticular</td>
<td>58.1</td>
<td>14.5</td>
<td>64.5</td>
<td>11.3</td>
<td>52.0</td>
</tr>
<tr>
<td>Thalamic</td>
<td>52.5</td>
<td>13.0</td>
<td>59.9</td>
<td>11.9</td>
<td>50.0</td>
</tr>
</tbody>
</table>

Mean values are milliliters per 100 grams per minute.
The ventrolateral nucleus projects onto the anterior motor and premotor cortical areas. The interruption of this circuit in the region of the cerebellar nuclei (or their connections) was possibly responsible for the CBF reduction in the hemisphere, predominating in the frontal structures. Nonetheless, a retrograde mechanism through an interruption of the corticopontocerebellar tracts could not be excluded. An argument in favor of this phenomenon was the observation in one patient of a decrease in the cortical CBF in conjunction with a paradoxical increase in thalamic rCBF. This increase could be linked with an abnormal activation of the thalamus by the cerebellar nuclei through the removal of the inhibitory effect exerted by the cerebellar cortex.  

The second phenomenon observed was a CBF reduction ipsilateral to the cerebellar lesion. It was more limited, chiefly involving the anterior frontal region, and was the reverse of the reduction in CBF and oxygen extraction previously described in the cerebellum ipsilateral to frontal lesions. Several mechanisms require discussion. Hydrocephalus can develop in the first few days after a cerebellar hemorrhage. However, in this study, the patients were examined at a stage at which they no longer displayed symptoms suggesting such a complication. The possibility of hypoactivity secondary to an extension of the lesions toward the vermis cannot be excluded. It is also possible that this phenomenon may be linked with the interruption of ipsilateral cerebellum–hemisphere tracts, the existence of which was suggested by anatomic studies.

According to the Von Monakow concept, diaschisis is a phenomenon that is transient, or at least continuously regressive in time, thus explaining the functional recovery. In our work, we have not observed any significant correlation between the time elapsed since the stroke and the rCBF values. This could represent an argument in favor of the stable nature of the reduction in CBF and metabolic activity. Nonetheless, the CBF studies were conducted within relatively short periods of time (13–79 days) after the strokes. In the crossed cerebellar diaschisis of hemispheric lesions, Baron et al suggested a progressive regression in their first work, but, in a later study, Pantano et al showed that hypoactivity persisted without any correlation with time after stroke. They have thus considered that these elements ran counter to the concepts of Von Monakow. Our data support their conclusions with regard to hemispheric diaschisis.

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