We studied the effect of acetazolamide on cerebellar blood flow in 11 stroke patients with large, unilateral cerebral hemispheric infarcts and no evidence of cerebellar infarction, but with cerebrocerebellar diaschisis of cerebral blood flow. Blood flow was determined with xenon-133 inhalation and dynamic single-photon emission computed tomography at rest and 20 minutes after the intravenous injection of 1.0 g acetazolamide. After acetazolamide, the mean±SD increases in blood flow in the affected and contralateral cerebellar hemispheres were 11.1±3.7 and 12.0±5.3 ml/100 g/min, respectively; the difference between hemispheres was not significant. The absolute increase in cerebellar flow in these 11 patients was of the same magnitude as that in 12 healthy controls. We conclude that cerebellar vasoreactivity is intact in stroke patients with crossed cerebrocerebellar diaschisis of cerebral blood flow. Our results lend further support to the concept that reduced cerebellar blood flow is secondary to functional deactivation. Our patients were studied 2 weeks to 5 years after their stroke, indicating that this phenomenon may be persistent. (Stroke 1990;21:52-55)

Infarction in a cerebral hemisphere may reduce blood flow and energy metabolism in the contralateral cerebellar hemisphere. The most important mechanism for this reduction appears to be neuronal depression secondary to damage of the corticopontocerebellar pathway. This phenomenon is termed crossed cerebrocerebellar diaschisis of cerebral blood flow (CBF).

Intravenous injection of acetazolamide increases CBF and cerebellar blood flow within minutes in normal subjects. The only known pharmacologic effect of acetazolamide is a potent, reversible inhibition of carbonic anhydrase. The drug seems to cross the blood-brain barrier, although slowly. The exact mechanism of action of acetazolamide on CBF is not clear. However, a decrease in cerebral pH due to inhibition of carbonic anhydrase in the brain, causing carbonic acidosis, has been suggested.

In patients with impaired cerebrovascular hemodynamic reserve, the response to acetazolamide in the affected perfusion territories is attenuated or abolished. Little is known about the vasoreactivity in cerebellar regions with an intact arterial supply but a decreased baseline blood flow (assumed to be caused by deactivation). To elucidate this, we studied the effect of acetazolamide on cerebellar blood flow in patients with crossed cerebrocerebellar diaschisis of CBF and hemiparesis due to cerebral infarction.

Subjects and Methods

We studied 11 hemiparetic stroke victims who had large, unilateral hemispheric infarcts mainly in the middle cerebral artery territory. All 11 patients had crossed cerebrocerebellar diaschisis of CBF without evidence of cerebellar infarcts. Patient selection was based on the clinical history, neurologic findings, cerebral computed tomography, angiography, and/or Doppler ultrasonography, and xenon-133 inhalation with dynamic single-photon emission computed tomography. Details are given in Table 1.

CBF was determined using xenon-133 inhalation and dynamic single-photon emission computed tomography (Tomomatic 64, Medimatic Inc., Copenhagen, Denmark) with three reconstructed transaxial slices. Each slice was 2 cm thick, with an interslice distance of 2 cm. Right and left cerebellar blood flow was determined from the lowest slice (orbitomeatal plane+2 cm), which contained only the cerebellum. The outline of the nonaffected cerebellar hemisphere was determined by visual inspection, and a region of

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<table>
<thead>
<tr>
<th>No./sex/age (yr)</th>
<th>Months since stroke</th>
<th>Size and location of infarct</th>
<th>Carotid angiography/Doppler ultrasonography findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/54</td>
<td>62</td>
<td>Large, R parietal</td>
<td>R ICA occluded, L ICA normal</td>
</tr>
<tr>
<td>2/F/57</td>
<td>40</td>
<td>Large, R temporal</td>
<td>R ICA occluded, L ICA normal</td>
</tr>
<tr>
<td>3/F/39</td>
<td>7</td>
<td>Large, R temporal</td>
<td>R ICA occluded, L ICA normal</td>
</tr>
<tr>
<td>4/M/55</td>
<td>32</td>
<td>Large, L temporal</td>
<td>Normal</td>
</tr>
<tr>
<td>5/M/60</td>
<td>19</td>
<td>Large, L temporal and parietal</td>
<td>L ICA occluded, R ICA normal</td>
</tr>
<tr>
<td>6/M/64</td>
<td>22</td>
<td>Large, R frontal and parietal</td>
<td>R ICA occluded, L ICA normal</td>
</tr>
<tr>
<td>7/M/40</td>
<td>13</td>
<td>Large, R temporal and parietal</td>
<td>R ICA occluded, L ICA normal</td>
</tr>
<tr>
<td>8/M/49</td>
<td>22</td>
<td>Large, L temporal and parietal</td>
<td>Normal</td>
</tr>
<tr>
<td>9/M/57</td>
<td>2</td>
<td>Large, R temporal</td>
<td>R ICA stenosis (&gt;50%), L ICA normal</td>
</tr>
<tr>
<td>10/M/56</td>
<td>3</td>
<td>Large, L parietal</td>
<td>L ICA occluded, R ICA normal</td>
</tr>
<tr>
<td>11/M/70</td>
<td>0.5</td>
<td>Two large infarcts, R anterior watershed and occipitoparietal</td>
<td>Normal</td>
</tr>
</tbody>
</table>

No., patient number; F, female; M, male; large, >2 cm; R, right; L, left; ICA, internal carotid artery.

TABLE 2. Baseline Regional Cerebral Blood Flow in 25 Normal Subjects

<table>
<thead>
<tr>
<th>Region</th>
<th>Right Mean±SD</th>
<th>Right Range</th>
<th>Left Mean±SD</th>
<th>Left Range</th>
<th>Mean Difference (right-left) Mean±SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebellum</td>
<td>60.4±7.5</td>
<td>46-74</td>
<td>61.2±7.2</td>
<td>51-79</td>
<td>-0.8±1.8</td>
<td>-4.5-4.0</td>
</tr>
<tr>
<td>Middle cerebral artery territory</td>
<td>63.5±7.0</td>
<td>54-77</td>
<td>61.1±6.7</td>
<td>51-75</td>
<td>2.2±2.0</td>
<td>1.5-6.6</td>
</tr>
</tbody>
</table>

Values are ml/100 g/min, not corrected for Pco₂.

interest (ROI) was drawn manually. A symmetric ROI was automatically placed over the affected cerebellar hemisphere. Hemispheric CBF was determined from Slice 2 (orbitomeatal plane+6 cm), which was divided into three right and left ROIs, corresponding approximately to the estimated perfusion territories of the anterior, middle, and posterior cerebral arteries. Measurements were carried out at rest and 20 minutes after the intravenous injection of 1.0 g acetazolamide dissolved in 10 ml distilled water. The acetazolamide was injected immediately after completion of the measurement of baseline CBF. The same ROIs were used in the measurements of baseline and postacetazolamide CBF. CBF was calculated as milliliters per 100 grams brain per minute, and the values were not adjusted for Pco₂. Tables 2 and 3 give relevant values from normal subjects. Further details of the method have been described. Results

The mean values of regional CBF and cerebellar blood flow, the responses to acetazolamide, and the differences between hemispheres are summarized in Table 4. The individual responses are given in Figure 1.

TABLE 3. Regional Cerebral Blood Flow Before and After Intravenous Injection of 1.0 g Acetazolamide in 12 Normal Subjects

<table>
<thead>
<tr>
<th>Region</th>
<th>Before Mean±SD</th>
<th>Before Range</th>
<th>After Mean±SD</th>
<th>After Range</th>
<th>Increase Mean±SD</th>
<th>Increase Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebellum</td>
<td>58.6±9.0</td>
<td>46-79</td>
<td>69.0±4.8</td>
<td>56-91</td>
<td>10.3±5.2</td>
<td>-1.0-18.0</td>
</tr>
<tr>
<td>Middle cerebral artery territory</td>
<td>58.8±6.9</td>
<td>46-71</td>
<td>74.1±8.2</td>
<td>59-88</td>
<td>15.4±5.0</td>
<td>5-23</td>
</tr>
</tbody>
</table>

Values are ml/100 g/min.
Middle cerebral artery territory CBF and cerebellar blood flow in the nonaffected hemisphere were not significantly different from those in normal subjects. Values in the affected hemisphere were significantly lower than those on the nonaffected side and those in normal subjects ($p<0.01$).

The acetazolamide-induced CBF increase in the affected middle cerebral artery territory was significantly lower ($p<0.01$) than that in normal subjects and that in the nonaffected hemisphere, whereas the response in the nonaffected hemisphere did not differ significantly from that in normal subjects. Neither the acetazolamide-induced absolute nor the relative cerebellar blood flow response differed significantly between hemispheres or from that in normal subjects.

**Discussion**

We used acetazolamide to test the vasoreactivity of the cerebral and cerebellar resistance vessels. We have previously shown that acetazolamide does not increase blood flow proportional to the baseline value in normal subjects, but rather causes approximately the same increase regardless of the baseline value or the vascular territory. Leinsinger et al have reported a negative correlation between acetazolamide-induced vasoreactivity and baseline blood flow. These findings are somewhat unexpected since reactivity to CO$_2$ generally tends to be directly rather than inversely proportional to baseline blood flow. Thus, testing the vasodilatory reserve capacity with CO$_2$ and acetazolamide do not seem to be directly comparable.

We presume that the full range of vasodilatory reserve is not tested by the intravenous injection of 1 g acetazolamide.

After acute stroke, CBF may be reduced in areas remote from the lesion (the area of diaschisis). In the contralateral hemisphere, the reduction in CBF tends to be highest in the homologous locus and CO$_2$ responsiveness there may be reduced. The severity of the remote effect varies directly with severity of the infarction and time after the ictus. Blood flows tend to return to normal within 1 month. The subject has recently been reviewed extensively.

Takano et al studied remote focal hypoperfusion in the ipsilateral sensorimotor cortex of patients during the subacute or chronic stage after a small capsular infarct. In the area of diaschisis, the vascular response to CO$_2$ was higher than in normal brain, not only when calculated as a percentage increase, but also when calculated in absolute terms. Thus, the CO$_2$ responsiveness in areas of diaschisis seems to differ during the acute and chronic stages.

To our knowledge, there are no reports on the cerebellar vasodilatory reserve capacity in patients with hemiparetic stroke and crossed transtentorial
diascisis. We found the cerebellar vasoreactivity to acetazolamide to be intact in such patients. In neither absolute nor relative terms was the blood flow increase in the affected cerebellar hemisphere significantly different from that in the nonaffected cerebellar hemisphere. All our patients had passed the acute stage of stroke when they were studied.

Baron et al\textsuperscript{2} were the first to report that infarction in a cerebral hemisphere may change blood flow in the contralateral cerebellar hemisphere. These authors suggested that cerebellar diaschisis is a transient phenomenon, although only a few of their patients were studied >2 months after the cerebral infarction. Later, Lenzi et al\textsuperscript{19} and Vorstrup showed that deactivation is a persistent phenomenon in patients with large hemispheric lesions. The findings in our patients, who were studied 0.5–62 (mean 20.2) months after their stroke, support the view that this phenomenon may be long-lasting. Vasoreactivity to acetazolamide, however, is intact.

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References

KEY WORDS • cerebral blood flow • tomography, emission computed • acetazolamide
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