Cerebral Blood Flow Asymmetries in Headache-Free Migraineurs

Steven R. Levine, MD, K.M.A. Welch, MD, James R. Ewing, MS, Rajiv Joseph, MD, and Giovanni D'Andrea, MD

Regional cerebral blood flow (rCBF) asymmetries were studied in controls and patients with common and classic/complicated migraine using $^{133}$Xe inhalation with 8 homologously situated external collimators over each cerebral hemisphere. Migraine patients as a group more frequently had posterior rCBF asymmetries than controls ($p<0.03$). Although there were no differences in the number of anterior rCBF asymmetries, migraine patients had 2 or more asymmetric probe pairs more often than controls ($p<0.02$). The posterior rCBF asymmetries, consistent with the site of activation of many migraine attacks, may be related to more labile control of the cerebral circulation. (Stroke 1987; 18:1164-1165)

The nature of the regional cerebral blood flow (rCBF) changes during a migraine attack have been studied frequently, although the basis of these changes remains to be ascertained. We recently reported asymmetries of rCBF during the headache-free period in a small series of patients with migraine; this article extends our previous report in a larger series of migraine patients with new measures designed to confirm and examine the location and frequency of the cerebral blood flow (CBF) asymmetries and is presented as further evidence for the instability of CBF control between migraine episodes.

Subjects and Methods

rCBF was measured in 63 individuals by use of the noninvasive $^{133}$Xe inhalation technique employing a system of 8 probe pairs (16 total probes) with external collimetry. Probes were carefully matched over homologous regions of the 2 cerebral hemispheres. Eighteen controls (ranging in age from 24 to 30 years), 18 common migraineurs (mean age 44.9±9 years), and 27 classic/complicated migraine patients (mean age 27.9±14 years) were studied. The classic/complicated migraine group comprised patients with a diagnosis of migraine plus transient focal neurologic deficit. Patients had their rCBF measured at least 2 weeks after the last migraine. No aspirin-containing products, nonsteroidal anti-inflammatory drugs, or caffeine had been taken for at least 10 days before the rCBF study. All 63 subjects had normal neurologic examinations, and all migraine patients had normal contrast-infused head computed tomography (CT) scans. All migraineurs satisfied the criteria set forth by the ad hoc committee for the classification of headache.

Mean rCBF for each of the 3 groups was calculated using the initial slope index (ISI) method of Risberg et al. The regional percent interhemispheric difference was calculated as the difference between paired ISI values divided by their mean value and expressed as percent of the denominator. Based on variations between subjects in the control group, the mean ± 2 SD of each probe-pair difference always fell within 7%. Therefore, if a probe-pair difference was >7%, the pair was designated “asymmetric.” Six probe pairs were positioned over the anterior circulation (inferior frontal, superior frontal, fronto-temporal, temporal, parietal-temporal, and parietal), and 2 were positioned over the posterior circulation (occipital and occipito-parietal).

Statistical Plan

We compared controls with migraineurs to evaluate any difference in the mean CBF and rCBF and the extent and locations of asymmetries. When significant

Table 1. Number of Subjects With 2 or More Asymmetric Probe Pairs

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>%</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>1 of 18</td>
<td>6%</td>
<td>p&lt;0.02</td>
</tr>
<tr>
<td>All migraineurs</td>
<td>17 of 45</td>
<td>38%</td>
<td></td>
</tr>
<tr>
<td>Common</td>
<td>7 of 18</td>
<td>39%</td>
<td></td>
</tr>
<tr>
<td>Classic/complicated</td>
<td>10 of 27</td>
<td>37%</td>
<td></td>
</tr>
</tbody>
</table>

Asymmetric probe pair: individual pair of probes that differ in initial slope index by >7%.
differences in demographics (sex, age, systolic blood pressure, diastolic blood pressure, hematocrit, and PCO2) arose, only mean CBF data was adjusted and controlled by regression analysis of continuous variables so these features would not contribute to differences in mean CBF between groups. Asymmetries were analyzed on the basis of the raw data. Two-sample t tests were used to compare migraineurs with controls for the continuous variables; Fisher’s exact tests were used for the categorical variables. The Bonferroni correction was used to add statistical rigor because of multiple testing on the same set of data. The values \( p < 0.05 - 0.03 \) were regarded as borderline significant; \( p < 0.025 \) was regarded as significant.

### Results

There was no significant difference between mean CBF in control subjects and migraineurs although a trend toward lower CBF was noted in the migraineurs \( (p < 0.05) \). When asymmetries were compared, 2 or more asymmetric probe pairs were found more frequently in migraine patients independent of migraine type than in controls \( (p < 0.02) \) (Table 1). No significant differences were seen in the number of patients with asymmetries in the anterior circulation, but posterior asymmetries were more evident \( (p < 0.03) \) (Table 2). Of possible interest, all 10 classic/complicated migraineurs found to have an asymmetric posterior probe pair also exhibited additional asymmetries in either the anterior or posterior circulation.

### Discussion

The use of a mean index of asymmetric blood flow during the headache-free period in migraine patients previously demonstrated the presence of rCBF asymmetries, but only in classic/complicated cases.4 In the present paper based on a different, independent index, we found asymmetries in both clinical types of migraine, and they were more frequently located in the posterior circulation. This may be relevant to the spreading oligemia reported during migraine attacks, which is generally thought to proceed from the occipital lobes forward, analogous to the spreading depression of neuronal function described by Leao.6

Whether these asymmetries are related the cause or the effect of migraine is uncertain. There are reports of persistent neurologic and neuropsychological deficits resulting from severe or frequent migraine attacks, but our patients had normal neurologic and head CT examinations, and asymmetries were seen as frequently in common as in classic/complicated migraine. Hockaday and Whittey previously failed to find any correlation between electroencephalographic abnormalities and migraine duration or severity. The measured asymmetries of CBF do not distinguish classic/complicated migraine from common migraine, nor do they support the concept that these are 2 different entities. However, if the asymmetries of blood flow are related to the cause of migraine, they could reflect an instability of CBF control.

### References


### Table 2. Asymmetries of Regional Cerebral Blood Flow

<table>
<thead>
<tr>
<th>Group</th>
<th>Number with asymmetric PP</th>
<th>%</th>
<th>p value</th>
<th>Number with asymmetric posterior PP</th>
<th>%</th>
<th>p value</th>
<th>Number with asymmetric anterior PP</th>
<th>%</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>7 of 18</td>
<td>39%</td>
<td></td>
<td>1 of 18</td>
<td>6%</td>
<td></td>
<td>6 of 18</td>
<td>33%</td>
<td></td>
</tr>
<tr>
<td>All migraineurs</td>
<td>29 of 45</td>
<td>64%</td>
<td>( p &lt; 0.1 )</td>
<td>16 of 45</td>
<td>36%</td>
<td>( p &lt; 0.03 )</td>
<td>24 of 45</td>
<td>53%</td>
<td>( p &lt; 0.18 )</td>
</tr>
<tr>
<td>Common</td>
<td>10 of 18</td>
<td>56%</td>
<td></td>
<td>6 of 18</td>
<td>33%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Classic/complicated</td>
<td>19 of 27</td>
<td>70%</td>
<td></td>
<td>10 of 27</td>
<td>37%</td>
<td></td>
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</table>

Asymmetric probe pair (PP): individual pair of probes that differ in initial slope index by >7%.

**Key Words**: cerebral blood flow • migraine • CBF asymmetries.
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