Cerebral Blood Flow and Neuropsychological Asymmetries in Unilateral Stroke

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Background and Purpose: This study sought to determine the degree of agreement between asymmetries of neuropsychological functioning and nine methods of quantifying asymmetries of regional cerebral blood flow.

Methods: The regional cerebral blood flow methods combined three markers of cerebral blood flow asymmetry (percent hemispheric difference, maximum percent probe-pair asymmetry, and number of probe-pair asymmetries) with three indexes of regional cerebral blood flow (fast compartment flow, initial slope index, and initial slope). Eleven patients with left hemispheric ischemic strokes and 13 with right hemispheric ischemic strokes were studied with the xenon-133 inhalation technique and neuropsychological tests.

Results: Blind clinical judgments of neuropsychological asymmetry significantly correlated with all nine methods of cerebral blood flow asymmetry determination; correlations ranged from -0.42 to -0.77. Clinical judgment of asymmetry of neuropsychological functioning accurately predicted the hemisphere of lower flow in 71–92% of cases, depending on the method of cerebral blood flow asymmetry determination. Agreement between cerebral blood flow and neurobehavioral signs of asymmetry was greater for initial slope and initial slope index than for the fast flow index. The initial slope and initial slope index showed equally good agreement. The use of the number of asymmetrical probe pairs to detect cerebral blood flow asymmetries agreed less well with neurobehavioral asymmetry than did the other two markers studied.

Conclusions: Both the initial slope index and the initial slope measures of cerebral blood flow are useful in predicting neuropsychological asymmetries, especially when the magnitude of the asymmetry is taken into account. (Stroke 1991;22:1384–1388)
Subjects and Methods

Of 58 patients with ischemic cerebrovascular disease who had regional cerebral blood flow studies and neuropsychological testing, a coauthor neurologist, experienced in the diagnosis of stroke, selected 24 patients with a history of thromboembolic stroke involving one hemisphere to a greater degree than the other. This decision was based on each patient's history, findings on neurological examination, computed tomography of the head, electroencephalography, and cerebral angiography. The neurologist was blind to each patient's regional cerebral blood flow and neuropsychological studies. As can be seen in Table 1, the typical patient was a male in his early 60s with a ninth- or 10th-grade education; all patients were right handed. There were no significant differences between the right and left hemispheric groups in age, education, or gender. The median time elapsed between patients' strokes and their blood flow studies was 2 months (range, 2 weeks to 78 months).

We used the xenon-133 inhalation technique for measuring regional cerebral blood flow. The xenon-133 was mixed with room air and administered via inhalation, in a concentration of 5 mCi/l, for a time of 1 minute, after which its clearance was monitored by a hemispheric array of \( \frac{34 \times 34}{3} \)-in. cylindrically collimated sodium iodide scintillation detectors. Pairs of detectors were placed symmetrically in the inferior frontal, superior frontal, frontotemporal, temporal, parietal, parietotemporal, occipitoparietal, and occipital regions of the left and right hemispheres. Robertson et al.\(^{10}\) can be consulted for a more complete description of probe placement. As in the procedures of Obrist et al.,\(^{10}\) we measured clearance for approximately 15 minutes. At approximately the second minute, when the concentration of inhaled radiogas reached 20\% of its peak value, we started the curve fitting for clearance rates, using the subsequent 10 minutes of data. We calculated three cerebral blood flow indexes: \( F_1, \)\(^{10}\) ISI,\(^{6}\) and IS.\(^{8}\)

Although we monitored end-tidal carbon dioxide in expired air throughout each study, we did not correct cerebral blood flow measures for carbon dioxide reactivity because carbon dioxide reactivity of infarcted brain regions is variable and differs from that of controls.\(^{11,12}\)

We developed three markers of hemispheric asymmetry: the percent hemispheric difference, maximum percent probe-pair asymmetry, and number of probe-pair asymmetries. The percent hemispheric difference was calculated by subtracting the mean flow of the left hemisphere (averaged over the eight probes) from the mean flow of the right hemisphere (averaged over the eight probes), dividing by the whole brain flow, and multiplying by 100. The two probe-pair markers were based on probe-pair ratios, which were calculated for each probe pair as follows:

\[
\frac{probe_{iL} - probe_{iR}}{(probe_{iL} + probe_{iR})/2} \times 100
\]

where probe\(_{iL}\) refers to the \( i \)th probe in the right hemisphere, and probe\(_{iR}\) refers to the symmetrical probe in the homologous region of the left hemisphere. Two markers of cerebral blood flow asymmetry were calculated from this equation. One marker, maximum percent probe-pair asymmetry, was the largest probe-pair ratio associated with any probe pair in a given subject. The sign of this value indicated the direction of the asymmetry, whereas the magnitude of the ratio indicated the degree of asymmetry. The hemisphere containing the lowest flow value of the most asymmetrical pair was identified as the ischemic hemisphere. The second marker, number of probe-pair asymmetries, was the number of probe pairs in which flow for the right-sided probe was greater than the left. The three markers of flow asymmetry varied in their sensitivities to regional low-flow states, with the maximum percent probe-pair ratio the most likely to detect focal low-flow states.

We performed a neuropsychological assessment within 5 days of the cerebral flow study, with an average length of delay of 1.6 days. The battery of neuropsychological tests was composed of the original or revised Wechsler Adult Intelligence Scale, the Wechsler Memory Scale, Hand Dynamometer, Finger Tapping Test and tests of finger gnosis and finger graphesthesia, as well as a confrontational assessment of visual fields.\(^{13}\) We selected these tests for study because neuropsychologists commonly use them to detect asymmetrical brain functioning.\(^{13,14}\) This battery also included several of the sensory and motor tests used in the neurological examination.\(^{15}\) Seven indicators of lateralized cerebral dysfunction were formed from the above tests. Two of these indicators were verbal IQ minus performance IQ and logical memory immediate recall minus visual reproduction immediate recall (from the Wechsler Memory Scale). Four other indicators were developed by subtracting the left hand score from the right on the hand dynamometer and finger tapping tests, and on tests of finger gnosis and finger dysgraphesthesia. A seventh score was formed by subtracting left visual field imperception errors
from right visual field errors. These seven difference scores accurately classified the laterality of 23 of the 24 patients studied. These seven difference scores accurately classified the laterality of 23 of the 24 patients studied.

Results

Tables 2 and 3 present results of the regional cerebral blood flow and neuropsychological studies. Although mean verbal and performance IQs were below the national mean, they were well within normal limits. There were no significant differences between patients with left or right hemispheric strokes for hematocrit or $PCO_2$. The mean blood flow values of the patients studied fell below our laboratory's normal range for people aged 50 and older.9

As seen in Table 4, multiple regression analysis indicated that the seven neuropsychological difference scores were correlated with several of the blood flow measures of asymmetry: ISI/percent hemispheric difference, ISI/maximum percent probe-pair, and the ISI/maximum percent probe-pair. Furthermore, the clinician's judgment of asymmetry of neurophysiological functioning significantly correlated with all nine regional cerebral blood flow measures of flow asymmetry (see Table 5). To determine how consistently flow measures of asymmetry predicted neurobehavioral asymmetry on a case-by-case basis, we performed a discriminant function analysis. For each discriminant function analysis, the clinician's judgment of the most involved hemisphere was the pre-
Table 5. Associations Between Cerebral Blood Flow and Clinical Ratings of Asymmetrical Cerebral Functioning

<table>
<thead>
<tr>
<th>Method for identifying hemisphere with cerebral blood flow asymmetry</th>
<th>Correlations with ratings of neurobehavioral asymmetry</th>
<th>Percentage of cases classified correctly*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Percent probe-pair maximum, ISI</td>
<td>-0.77†</td>
<td>92</td>
</tr>
<tr>
<td>2. Percent probe-pair maximum, IS</td>
<td>-0.65†</td>
<td>87</td>
</tr>
<tr>
<td>3. Percent probe-pair maximum, F1</td>
<td>-0.42‡</td>
<td>71</td>
</tr>
<tr>
<td>4. Probe-pair number, ISI</td>
<td>-0.64†</td>
<td>68</td>
</tr>
<tr>
<td>5. Probe-pair number, IS</td>
<td>-0.71†</td>
<td>76</td>
</tr>
<tr>
<td>6. Probe-pair number, F1</td>
<td>-0.42‡</td>
<td>64</td>
</tr>
<tr>
<td>7. Percent hemispheric difference, ISI</td>
<td>-0.68†</td>
<td>88</td>
</tr>
<tr>
<td>8. Percent hemispheric difference, IS</td>
<td>-0.65†</td>
<td>75</td>
</tr>
<tr>
<td>9. Percent hemispheric difference, F1</td>
<td>-0.62†</td>
<td>71</td>
</tr>
</tbody>
</table>

*In each discriminant function analysis, neurobehavioral ratings served as the predictor of asymmetry and cerebral blood flow measures as the criterion.

**Discussion**

For most of the analyses considered, the fast flow index, F1, was not strongly related to asymmetries of neuropsychological functioning. The fast flow index is known to be relatively unstable in stroke because edema, abnormal flow gradients, and other effects of stroke often add pathological flow compartments to the gray and white matter compartments of physiologically normal regional cerebral blood flow. When the two-compartment model is fit to flow data representing more than two flow rates, the additional rates of flow are partitioned between the two compartments. Large shifts between the estimates of rates of flow in the fast and slow compartments can occur as a result of modest changes in signals coming from pathological regions of the brain. Our data indicate that the instability of F1 is sufficiently great to make it an unacceptable marker of cerebral blood flow asymmetries in stroke. Both the ISI and IS are more stable in stroke, and measures of flow asymmetry based on either index were more strongly correlated with neuropsychological asymmetry than the F1 measures.

We also compared three markers of cerebral blood flow asymmetry. Merely counting the number of asymmetrical probe pairs appeared to be the weakest approach to identifying the stroke hemisphere. This method seemed particularly insensitive to the presence of marked but focal asymmetries of flow. Markers that reflect the intensity of flow asymmetries appear more sensitive to the effects of lateralized stroke than markers that reflect the pervasiveness of the asymmetry.

The clinical judgment of neuropsychological asymmetry and the ISI/percent probe-pair measure of asymmetry disagreed in only two cases. Both patients had neuropsychological and cerebral blood flow studies completed on the same day. One of these patients had a history of transient ischemic attacks and computerized tomography of the head suggesting a right hemispheric infarction. The regional cerebral flow study did indicate a relative reduction in right frontal flow. The neuropsychological testing revealed no deficits, a finding that corresponds with the patient’s transient symptoms. The second patient had a right hemispheric stroke 1 year before he was studied. He showed no clear flow asymmetry suggestive of either hyperemia or oligemia, even though he had a left hemiplegia at the time of the assessment. All probe-pair ratios were within the normal range; six of the probe pairs pointed to lower flow in the uninvolved left hemisphere. This patient represents a false-negative for the cerebral blood flow technique, presumably because the methods used could not resolve the patient’s low-flow abnormality in a chronic state. When the historical/neurological and neuroradiological findings to identify the stroke hemisphere were used, the ISI/percent probe-pair measure correctly identified the stroke hemisphere in all but one patient.

Overall, the results of this study support the use of regional cerebral blood flow methods as a valuable predictor of neurobehavioral asymmetry, that is, the ISI/maximum percent probe-pair measure.
noninvasive method of corroborating signs of later-
alized cerebral dysfunction found on neuropsy-
chological and neurological examinations.

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