Flow and Compartmental Weight in Relation to the Course of Stroke

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SUMMARY Using a scintillation camera system, hemispheric and regional cerebral blood flow was measured repeatedly during the course after a stroke. In 20 patients who improved clinically mean hemispheric and regional flow and relative weight of rapidly perfused compartment increased, while these values decreased in 15 patients, on an average, whose clinical condition deteriorated or did not change. The changes of flow and relative weight were significantly different between the two groups. Furthermore, the relationship between changes in clinical condition, scored according to a rating scale, and changes in flow and compartmental weight was proved by significant Spearman rank correlation coefficients. In six cases hyperperfused areas in locations of disturbed neurological function were observed; these areas were found to be ischemic at measurements done early and late in the course after the stroke. This type of hyperperfusion was related to beneficial prognosis.

The results indicate a shift of tissue from fast to slowly cleared compartment after a cerebrovascular attack. If tissue morphology is not entirely destroyed, recovery might occur; this results in an increase of recorded weight of rapidly clearing compartments, which correlates to the clinical course.

IN EXPERIMENTAL OCCLUSION of the middle cerebral artery, blood flow is initially reduced in the infarcted area and consequently may change in relation to the evolution and resolution of neurological defects. In patients having strokes due to local ischemic perfusion, changes related to the clinical course were observed by means of invasive and noninvasive methods. As was shown in previous investigations, changes in flow may have an impact on the distribution of the compartments as calculated by bicompartamental analysis. These observations led to the conclusion that the rapidly and slowly clearing compartments are not morphological entities but dynamic ones, which may show a varying degree of overlap. Thus, we wished to investigate whether changes in flow and compartmental weight were related to the clinical course of patients after cerebrovascular ischemia (CVI).

Methods

The study was based on data obtained from 35 patients, age 15 to 72 years, who had CVI of acute or progressive onset and of varied severity, ranging from transient ischemic attacks to complete hemiplegia and aphasia. In all cases ischemic cerebrovascular disease was diagnosed based on clinical data and laboratory findings such as EEG, scintigraphy, CSF examination and cerebral angiography, which revealed unilateral carotid occlusion in four, carotid stenosis in five, carotid kinking in three, middle cerebral artery (MCA) occlusion in six, MCA stenosis in three, occlusion of MCA branches in three and moderate diffuse arteriosclerosis of cerebral vessels in 11 cases. All patients received similar conservative treatment consisting of intravenous infusions with low molecular dextran, heoxbendine, cardiac glycosides and dehydrating agents. If necessary, electrolytes were balanced and diabetes, infections and renal or cardiac insufficiency were treated. With all patients physiotherapy was started immediately with passive movements and positioning of plegic limbs; the patients entered into an active program as soon as possible. The clinical course was followed up by a three-point rating scale: disturbance of motor function from absent = 0 to complete plegia of limbs = 3; disturbance of higher brain functions from absent = 0 to complete deficit (e.g., aphasia) = 3; mental dysfunction from absent = 0 to severe psycho-organic syndrome = 3. The sum of the ratings in the three categories yielded a score for the clinical condition and was used to estimate improvements semiquantitatively. An improvement was defined as diminution of total score by two or more points or change from one to zero of total score.

Hemispheric and regional cerebral blood flow (CBF) was investigated by use of a modified version of the isotope clearance method. Under local anesthesia the internal carotid artery was punctured and 4 to 10 mCi of 133 xenon in saline solution (1 to 2 ml) were injected rapidly. The gamma activity in the brain was recorded by an Anger type scintillation camera placed on one side or on the vertex of the head in cases with carotid occlusion, in which the isotope was injected via the opposite internal carotid artery, and sufficient count rates were obtained due to a cross flow. Scintiphotos taken during the first seconds after injection proved the selective injection into the internal carotid artery without extracranial contamination. A dual ratemeter and a writer directly registered analogue washout curves from one or both hemispheres. The impulses from the camera were fed simultaneously to a dual ADC and a 1,600-word memory. This memory sampled the information in periods of 2.4 seconds for the first and second minute, and in periods of 18 seconds for the third to tenth minute after xenon injection and placed these 70 individual frames into a digital magnetic tape. The data were processed off-line on an IBM 1800 system. For brain areas of 12 x 12 mm the computer calculated the following flow parameters: \( f_b \) is the weighted flow from bicompartamental analysis (\( f_b = W_1 \cdot f_1 + W_2 \cdot f_2 \)); \( f_1 \) is the flow of rapidly perfused compartment; \( f_2 \) is the flow of the slowly perfused compartment (all in ml/100 gm per minute), and \( W \) is the relative weight of rapidly perfused compartment (in percent). The results were printed in the form of two-dimensional flow maps. Flow also was calculated according to stochastic analysis (\( f_s \)). In all cases \( f_s \) was close to \( f_b \) and was used as a control for the values obtained from biexponential analysis. Therefore, \( f_b \) is not given further in this communication.

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Supported by the Österreichischer Fonds zur Förderung der wissenschaftlichen Forschung and by the Jubiläumsstiftung der Österreichischen Nationalbank.
The first measurement of CBF was usually performed 1 to 30 days after the first cerebrovascular attack; in eight patients the studies were done later (in three cases 60, in others 84, 90, 120, 180 and 440 days after the first stroke), but within one to two weeks after a new deterioration in the clinical state of these cases. Brain perfusion was studied again after 7 to 45 days; in five cases the interval between the two measurements was between 0.5 and two years. None of the cases had a new cerebrovascular accident between the two CBF studies. The clinical condition was rated independently on the day of the CBF study. Arterial carbon dioxide tension (Paco2) was measured before each CBF registration and was within the normal range in all instances.

Results

According to the change in the clinical score between the two CBF studies the patients were categorized into two groups: the first group of 20 patients had an initial mean score of 5.3 and improved by 3.3; the 15 patients of the second group had an initial score of 4.7 and these cases showed no marked improvement or deterioration, yielding an average change of score by +0.8. Due to the use of this variable as the classifying criterion, the changes in the scores of the two groups were significantly different (table 1). The results of the hemispheric perfusion studies are summarized in table 1. There was no difference in the mean flow values between the patients who had clinically improved and the ones who had not, but the changes in these values, shown at the second investigation, were different from each other in the two groups. In the patients who had clinically improved, f1 and W1 increased markedly, while f2 and d1 did not change very much. The contrary was found in the patients who had not improved clinically: in this group the flow values decreased. The mean changes in the flow parameters of the two groups between the first and the second measurement were compared by Student's t-test: the changes of f1 and W1 were significantly different (P < 0.01), while the change in f2 was not and the change in W2 was only slightly (P < 0.05) different.

Regions with further impaired blood supply, which corresponded to the site of the neurological symptoms, were found in 14 patients who improved clinically and in 14 cases whose clinical state deteriorated or did not change. These regions were arbitrarily indicated (figs. 1 and 2), defining areas of interest. Calculation of average flow and compartmental weight within these areas was based on the flow maps obtained from different studies. Mean values and standard deviations of flow values and weight of rapidly clearing compartments in these regions at the first measurement and their

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**TABLE 1 Clinical Course and Hemispheric Flow Changes**

<table>
<thead>
<tr>
<th>Clinical score</th>
<th>f1 (ml/100 gm • min)</th>
<th>f2 (ml/100 gm • min)</th>
<th>W1 (%)</th>
<th>W2 (%)</th>
<th>Pco2 (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved (N = 19)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>5.3 ± 2.1</td>
<td>34.2 ± 5.3</td>
<td>54.0 ± 7.6</td>
<td>21.9 ± 3.3</td>
<td>38.6 ± 7.8</td>
</tr>
<tr>
<td>Change</td>
<td>-3.3 ± 1.3</td>
<td>+7.5 ± 14.4</td>
<td>+2.7 ± 16.0</td>
<td>-2.4 ± 10.7</td>
<td>+17.1 ± 29.9</td>
</tr>
<tr>
<td>Not improved (N = 15)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>4.7 ± 2.6</td>
<td>35.2 ± 5.0</td>
<td>54.1 ± 5.9</td>
<td>21.8 ± 2.6</td>
<td>41.4 ± 7.7</td>
</tr>
<tr>
<td>Change</td>
<td>0.8 ± 1.7</td>
<td>-9.0 ± 13.3</td>
<td>-1.4 ± 18.3</td>
<td>-11.4 ± 11.0</td>
<td>-10.4 ± 12.5</td>
</tr>
</tbody>
</table>

Changes in clinical score and in Pco2 are given in absolute values, and changes in flow values are in percent.
percent changes during the observation period are given in table 2. Again, the mean flow values at the first measurement were not different from each other in the two groups, but \( f_n \) and \( W_i \) showed significantly different changes (\( P < 0.01 \)) in relation to the clinical course, while the differences in the changes of \( f_1 \) and \( f_2 \) did not reach a level of statistical significance.

Maps of regional flow and compartmental weight of typical cases of the two respective groups are shown in figures 1 and 2: The patient whose charts are demonstrated in figure 1 improved clinically from a score of 7 to a score of 2. The maps indicate a region with further impaired blood supply and decreased relative weight of rapidly perfused area. The obtained correlation coefficients are given in table 3 together with the levels and limits of statistical significance. This analysis also proved the significant relation between flow and compartmental weight changes and clinical course.

In five patients (four with clinical improvement and one without) hyperperfused (areas whose mean value was, in t-test, significantly above the surrounding hemisphere) instead of ischemic regions were observed in brain areas corresponding to the location of disturbed neurological functions. In four of these cases two additional measurements were performed in which ischemic regions were detected in the place of the hyperperfused areas. These measurements with detectable ischemic foci were used for statistical analysis. One of these cases, with clinical improvement by four points, in which an ischemic focus was found on the third and twenty-fourth day and a hyperperfused focus on the tenth day, is shown in figure 3. A similar temporal course (ischemic lesion on the third and twenty-third day and hyperperfused area on the tenth day) was seen in a second patient. In a third case (a transient MCA occlusion) a hyperperfused region (\( f_n = 74.1, f_1 = 100.2, f_2 = 25.7, W_i = 64.2 \)) observed on the thirteenth day returned to normal values 40 days after the attack (\( f_n = 52.2, f_1 = 74.1, f_2 = 26.1, W_i = 49.8 \)). This case was not included in the statistical calculations. In the fourth case the hyperperfused area was found at a third measurement done after successful endarterectomy of carotid artery stenosis. In the only case without clinical improvement the hyperperfused area

![Figure 2](https://example.com/figure2.png)

**Figure 2.** Maps of tissue flow and percentage weight of rapidly perfused compartment in a patient with dysphasia, hemiparesis and hemihypesthesia due to stenosis of middle cerebral artery. This clinical condition did not improve (score from 3 to 4), and the flow values deteriorated between the twelfth and the thirty-first day after the stroke.

### Table 2: Regional Flow Changes in Improved and Not Improved Patients

<table>
<thead>
<tr>
<th></th>
<th>( f_n ) (ml/100 gm * min)</th>
<th>( f_1 ) (ml/100 gm * min)</th>
<th>( f_2 ) (ml/100 gm * min)</th>
<th>( W_i ) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved (N = 14)</td>
<td>31.3 ± 4.6</td>
<td>48.8 ± 7.3</td>
<td>19.9 ± 2.3</td>
<td>37.8 ± 6.7</td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% change</td>
<td>+9.5 ± 19.6</td>
<td>+4.0 ± 19.4</td>
<td>+7.5 ± 10.1</td>
<td>+14.1 ± 23.4</td>
</tr>
<tr>
<td>Not improved (N = 14)</td>
<td>32.2 ± 13.3</td>
<td>55.1 ± 20.1</td>
<td>20.8 ± 3.8</td>
<td>36.5 ± 9.9</td>
</tr>
<tr>
<td>% change</td>
<td>-10.8 ± 18.3</td>
<td>-2.2 ± 25.5</td>
<td>-5.5 ± 25.0</td>
<td>-16.9 ± 24.2</td>
</tr>
<tr>
<td>Comparison of % change</td>
<td>t = 2.89</td>
<td>0.72</td>
<td>1.04</td>
<td>3.45</td>
</tr>
<tr>
<td>P &lt;</td>
<td>0.01</td>
<td>-</td>
<td>-</td>
<td>0.01</td>
</tr>
</tbody>
</table>
TABLE 3 Spearman Rank-Correlation: Changes in Clinical Score Versus Changes in Flow Values

<table>
<thead>
<tr>
<th>Correlation coefficient</th>
<th>P &lt; Limit of significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>fh</td>
<td>0.451</td>
</tr>
<tr>
<td>fr</td>
<td>0.535</td>
</tr>
<tr>
<td>Wh</td>
<td>0.519</td>
</tr>
<tr>
<td>Wf</td>
<td>0.525</td>
</tr>
</tbody>
</table>

fh: IB of the hemisphere; fr: mean fb in the ischemic region; Wh: IB of the hemisphere; and Wf: mean Wf in the ischemic focus.

In this paper results of repeated CBF measurements in stroke patients are presented. To avoid the transient changes of CBF in the acute stages after a cerebrovascular accident, the first measurements were performed at a time at which the clinical condition was stabilized. CBF was studied again after an observation period and the flow changes were correlated to the change in the clinical condition during this time. Improvement or deterioration occurring after the observation period was not taken into consideration. As shown in the results, changes of hemispheric and regional flow and compartmental weight are related to the clinical course during the observation time after a stroke. A similar relation between clinical course and changes in flow and compartmental weight was described by Salmon and Timperman in patients with head injury before and after ventriculo-atrial shunting. In the group of patients with worsening or nonimproving clinical deficits, flow and relative weight of rapidly cleared compartments (Wt) decreased. This change of Wt could be due to a further loss of tissue in the rapidly perfused compartment, which could be caused by persisting impaired blood supply, metabolic changes based on perifocal edema, atrophy, etc. This substantial loss would explain the clinical worsening. However, the contrary cannot be true for the increase of hemispheric and regional Wt.

Discussion

The two-compartmental exponential model is based on the assumption of two distinct differently cleared compartments, one with a fast clearance, considered to be cerebral gray matter, the other with a slow clearance, considered to consist mainly of white matter. In unimpaired brains, where the difference in perfusion between gray and white matter is at least fourfold, the distinction between the clearance rates of slowly and rapidly perfused tissue is strict and without overlap. In certain pathological states with intermediate flow rates (mainly altered gray tissues) seem to fluctuate between the two compartments and to induce a shift of compartmental boundaries. Such fluctuations causing changes in the weight of the compartments were observed in patients with cerebrovascular disease when CBF was acutely increased or decreased by varying PCO2. The same occurred in patients with head injuries when alterations of CBF were produced by altering systemic arterial pressure or by giving intravenous mannitol infusions.

FIGURE 3. Maps of tissue flow and percentage weight in a patient with expressive aphasia, hemiplegia, hemihypesthesia and psychoorganic syndrome due to stenosis of the middle cerebral artery. The clinical condition improved (score from 8 to 4); the maps show an ischemic region on the third day after the attack, a hyperperfused area on the tenth day, and an improved ischemic region on the twenty-fourth day after the attack.
observed in the group of patients with clinical improvement. In these cases parts of the compartment usually rapidly perfused have flow values which lie in the range of the values of the slowly cleared compartment. This phenomenon is visible at a time after a cerebrovascular attack when the strict distinction between the two compartments no longer exists. If the morphology of these slowly perfused parts of the compartment usually rapidly cleared is not entirely destroyed during the ischemic attack, they might recover. This is shown in the increase of recorded $W$, and explains the clinical improvement.

Another interesting result of our study is the comparatively high incidence of hyperperfusion observed in foci of disturbed neurological function in patients showing clinical improvement. This hyperperfusion which was seen between the sixth and thirteenth day in four out of the six cases seems to be different from the luxury perfusion\textsuperscript{16,17} in acute stages after a stroke, but might be comparable to the late hyperperfusion observed in experimental MCA occlusion.\textsuperscript{1} In contrast to an early hyperperfusion occurring during the first 24 hours after MCA occlusion, late hyperperfusion had a beneficial effect on the improvement of neurological deficits. The occurrence of hyperperfused patches as a sign of favorable prognosis was also indicated by a correlation analysis of flow data, neurological deficits and clinical course in patients with obstructive neck vessel disease.\textsuperscript{18} Together with these reported results our data suggest that this type of hyperperfusion is an effective mechanism for improving perfusion in ischemic brain lesions.

References


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Stroke. 1976;7:399-403
doi: 10.1161/01.STR.7.4.399

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