No Evidence for Transhemispheric Diaschisis After Human Cerebral Infarction

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SUMMARY Forty-four studies of regional cerebral blood flow (rCBF), fractional oxygen extraction (rOER) and oxygen consumption (rCMRO₂) were made on twenty-five patients with recent internal carotid artery territory infarcts. The purpose was to study flow-metabolism relationships in the contralateral hemispheres, and to investigate whether contralateral rCMRO₂ was depressed as a result of the recent infarcts. Two groups of controls were included for comparison — seventeen normal volunteers, and ten patients with proven extracranial cerebrovascular disease but without evidence of cerebral infarction. The results demonstrated that: 1) contralateral hemispheric rCMRO₂ was less variable than regional oxygen availability (the product of rCBF and arterial oxygen content). This was due, in part, to the effect of individual variations in PaCO₂ on rCBF, but other uncontrolled factors, such as intracranial pressure, may have had influences. As a result, rCMRO₂ did not correlate with rCBF; 2) mean rCMRO₂ in the contralateral hemispheres was 12% lower than normal (a significant difference), but was not different from the value found in patients with extracranial vascular disease in whom there was no evidence of infarction or ischemia; 3) contralateral rCMRO₂ did not correlate with the size of the infarct in the opposite hemisphere. It is concluded that rCMRO₂ cannot be inferred from rCBF measurements in uncontrolled human studies (as frequently done in the past), and that depression of contralateral rCMRO₂ may have preceded infarction in the opposite hemisphere, a consequence of the previous influences of diseases that predispose to stroke.

Stroke Vol 17, No 5, 1986
logically intact subjects with a profile of risk factors predisposing to stroke similar to that present in the patients. Such a comparison would exclude the effects of chronic hypertension, extracranial vascular disease, etc. on rCBF and rCMRO₂, and the remote effects of an acute hemispheric infarct alone could be ascertained.

With these considerations in mind, this study set out to answer two questions:

1. Is there a similar reduction in oxygen supply and demand in the cerebral hemisphere contralateral to a recent cerebral infarct, as frequently assumed in the past?
2. If rCMRO₂ is reduced in the contralateral hemisphere, can this confidently be attributed to a remote effect of the infarct?

**Methods and Data Analysis**

**Scanning Procedure**

All patients were scanned on the ECAT-II²⁸ positron emission tomographic scanner, with a measured resolution of 16.7 x 16.7 x 16.7 mm³ (full width, half maximum). A description of the ECAT-II²⁸ scanner has been published. The scanning procedure was the same as detailed in a previous publication. The scans were performed at planes parallel to the orbito-meatal (OM) line. Two planes were studied, through the levels of the lentiform and thalamic nuclei (OM + 4.0 - 4.5 cm) and the centrum semiovale (OM + 6.0 - 6.5 cm).

**Tracer Techniques**

The ¹⁵O steady-state inhalation technique was used, in combination with PET, to measure CBF, OER and rCMRO₂. This technique has been subjected to detailed analysis. The majority of studies included radial artery cannulation, which permitted multiple arterial samples during each period of steady-state inhalation of tracer and, therefore, greater accuracy in the estimation of blood tracer concentration. Most studies also included an estimation of regional cerebral blood volume (rCBV), using carbon-11 monoxide (¹¹CO) as tracer. It has been shown that rOER is overestimated if no correction is made for signal from unextracted hemoglobin-bound ¹⁵O during scanning whilst the patient inhales molecular ¹⁵O₂. rCBV estimations allowed correction of rOER for this error. Inclusion of a ¹¹CO scan in an individual study was dependent upon the availability of tracer from the cyclotron, and not upon a constant pathological factor such as the patient's conscious level.

**Data Analysis**

Computer printouts were obtained for regional values of CBF, OER and CMR₀₂. Each number in the numerical matrix represented the mean value of 3 x 3 pixels, that is an area of brain in the transaxial plane of 0.75 x 0.75 cm². 'Cortical strips' were defined on these matrices by a method previously described. Such 'cortical strips' will have included subcortical white matter because of convolutions of the cortex and the limited resolution of the scanner. The minimum width for defining the cortex on the cortical plots was chosen as the best compromise between the physical dimensions of the anatomical elements of the brain and the resolution of the ECAT-II²⁸ scanner. Heterogeneity of tissue within individual pixels will have resulted in an underestimation of mean rCBF (up to a maximum of 18%), although estimation of rOER was not subject to this error. The method of cortical strip analysis provided an objective means of identifying similar regions from the studies on each patient, and the errors imposed by the limited resolution of the scanner would have been of similar order for each study.

The ¹⁵O steady-state technique relies on constant tissue and blood tracer concentration during scanning. Fluctuations in tracer concentration can arise both from errors in methodology (for example, irregular respiration by the patient) and from changes in cerebral physiology during the course of a study. To exclude studies which were clearly not steady-state, a comparison was made of 'cortical' OER, CBF and CMR₀₂ between planes in the hemisphere contralateral to the infarct. In the absence of focal pathology or focal activation in this hemisphere it was to be expected that the variables would be similar between planes in a steady-state study. On this basis studies were rejected if OER contralateral to the infarct varied by more than 10% between the two supratentorial planes, or if CBF or CMR₀₂, varied by more than 15% (with the difference between planes expressed as a percentage of the plane with the lower value of the variable). The thickness of the cortex is not constant throughout a cerebral hemisphere, and varying proportions of gray and white matter included in the cortical plots will have been a source of minor inter-plane variations in 'cortical' CBF and CMR₀₂. This does not apply to comparisons of 'cortical' OER as it is normally similar in gray and white matter; therefore, the slightly greater limit was permitted for inter-plane variations in rCBF and rCMR₀₂.

Ideally, the steady-state should have been confirmed directly by continuous monitoring of arterial blood radioactivity. This was not ethically permissible, as it would have required either the steady withdrawal of blood for ten minutes (a large volume of blood) or the insertion of an arteriovenous shunt. The indirect method used to exclude studies was based on differences of the variables between planes (up to 30%) that were largely diffuse. There was no instance encountered of a marked functional difference in a focal region within one plane resulting in exclusion of the study by the criteria employed — such a finding would have more properly been considered an example of extreme regional activation or inhibition, or of local disease.

The limits for inter-plane functional differences that were used are arbitrary. There were a large number of exclusions amongst the stroke patients (twelve studies on eight patients), as it may be difficult to achieve a steady-state in recently disabled, anxious, often aphasic patients. There was a danger that these exclusions could have resulted in rejection of a valid observation.
This does not appear to be the case — the key observation was the value of ‘cortical’ CMRO₂ in middle cerebral artery territory contralateral to the infarcts, and the mean value in the rejected studies (2.8 ± 0.4 ml/100 ml/min) was the same as in the forty-four studies included in this series (2.8 ± 0.3 ml/100 ml/min).

The mean of the ‘cortical’ values for the two planes are presented in the results.

Dosimetry

The radiation exposures to the whole body and to vulnerable organs during a two plane study have been tabulated by Rhodes et al.²⁶ Typical blood concentrations during C15O₂ and ¹⁵O₂ inhalation and after ¹⁵CO inhalation were determined from patient studies done at the MRC Cyclotron Unit, Hammersmith Hospital.

Patients and Controls

Patients

Forty-four studies on twenty-five patients with acute, unilateral cerebral infarction within carotid artery territory were included in this study. Thirty-three of the studies included rCBV estimations. All patients had X-ray CT scans to confirm the clinical diagnosis of hemispheric infarction, and to exclude the presence of lesions in the cortex of middle cerebral artery territory of the contralateral hemisphere, the region selected for analysis. The individual infarcts varied in size from an internal capsular lacune to destruction of most of the territories of anterior and middle cerebral arteries. Details about the patients and the X-ray CT scan findings are summarized in table 1.

Controls

Two groups of controls were used:

Seventeen normal volunteers. Ten were elderly volunteers used as normal controls in a previous study on dementia.²¹ These studies did not include rCBV estimations, and arterial blood samples were drawn by single arterial puncture during the inhalation of ¹⁵O₂ and C¹⁵O₂. A further seven younger volunteers were recruited, and their studies included radial artery cannulation and rCBV estimations. The magnitude of rCBV-correction of rOER and rCMRO₂ in middle cerebral artery territory cortex was 12 ± 2% at OM + 4 cm and 10 ± 2% at OM + 6 cm. These mean corrections were applied to the individual data from the older controls to give estimated rCBV-corrected rOER and rCMRO₂ in these subjects. As the percentage correction of rOER, and hence rCMRO₂, depends on the individual values of rCBV, rCBF and rOER,¹⁹ the estimated correction of the data from the elderly volunteers will have been a source of small error — but considerably less than the 10—12% error if no rCBV-correction was applied.¹⁹

Ten patients with extracranial vascular disease but without evidence of cerebral infarction. This group came from the series of Gibbs et al.²² and comprised patients with major extracranial vascular disease but without clinical evidence of cerebral infarction. Six had X-ray CT scans, which were normal. The four that did not have X-ray CT scans had never experienced cerebral symptoms (one being asymptomatic and three having a history of retinal ischemia only). All ten had normal neurological examinations. The studies on these patients included radial artery cannulation and rCBV estimations. Clinical and radiological details are summarised in table 2.

The individual ‘cortical’ values used were the mean of both cerebral hemispheres. It was the values of rCMRO₂ that were of particular interest. ‘Cortical’ CMRO₂ tended to be a little lower ipsilateral to the occluded internal carotid artery (ICA), but the difference between the means of the two hemispheres, that is ipsilateral and contralateral to the occluded ICA, were not significant. In the larger series of Gibbs et al²² this difference remained statistically insignificant. ‘Cortical’ OER was a little higher (not significantly) on the side of the occluded ICA — this reached statistical significance in the larger series of Gibbs et al,²² although it only amounted to a 7% difference.

The studies on the patients with extracranial cerebrovascular disease without established infarction were done at least several weeks (in many cases several months) after the last transient ischemic attack. ‘Cortical’ CMRO₂ did not correlate with the type of transient ischemic attack.

A comparison of mean subject age and the means of a number of physiological variables between the patient and two control groups is presented in table 3.

The purpose and nature of the study were approved by the Hammersmith Hospital Research Ethics Committee and the United Kingdom Administration of Radioactive Substances Advisory Committee. Informed consent was obtained prior to study from all volunteers and patients, or informed assent from the closest relative in the case of asphasic patients.

Results

Regional oxygen supply and demand are linked by the relationship:

\[ r\text{CMRO}_2 = r\text{CBF} \times \text{CaO}_2 \times r\text{OER} \]

where \( \text{CaO}_2 \) is the arterial oxygen content, and the product of \( r\text{CBF} \) and \( \text{CaO}_2 \) is the rate of oxygen supply (oxygen availability).

There was a relationship between rOER and regional oxygen availability \( (r\text{O}_2\text{Av}) \) in the hemispheres contralateral to the infarcts (fig. 1). The linear negative correlation was significant \( (r\text{OER} = 0.76 - 0.44 r\text{O}_2\text{Av}; r = -0.74; p < 0.0001, \) by two-tailed t test).²⁶ although inspection of the scatter diagram suggests that the inverse relationship may be even better described by a gentle curve. Given the relationship between oxygen supply and demand described above,

\[ r\text{OER} = 0.75 - 0.046 r\text{O}_2\text{Av}; r = -0.75. \]

*Eleven of the forty-four rOER data points were uncorrected for rCBV (see Methods). Mean measured rCBV-correction of the other thirty-three was 9 ± 3%. The relationship remained significant if a correction of 9% was applied to the eleven uncorrected rOER values \( (r\text{OER} = 0.75 - 0.046 r\text{O}_2\text{Av}; r = -0.75). \)
TABLE 1  **Details on Stroke Patients**

<table>
<thead>
<tr>
<th>Patient No.*</th>
<th>Timing of PET scans from ictus</th>
<th>Presenting signs</th>
<th>X-ray CT scan appearances</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>4 days</td>
<td>R hemiparesis</td>
<td>Equivocal L internal capsular infarct</td>
</tr>
<tr>
<td>4</td>
<td>18 hours</td>
<td>L hemiparesis</td>
<td>R internal capsular infarct</td>
</tr>
<tr>
<td>5</td>
<td>2.5 days</td>
<td>Non-fluent dysphasia</td>
<td>Extensive L MCA territory infarct</td>
</tr>
<tr>
<td>8</td>
<td>5.5 days</td>
<td>R hemiplegia</td>
<td>Extensive L ACA and MCA territories infarct</td>
</tr>
<tr>
<td>7</td>
<td>2 days</td>
<td>Global aphasia</td>
<td>Extensive L MCA territory infarct</td>
</tr>
<tr>
<td>3</td>
<td>3 days</td>
<td>R h. hemianopia</td>
<td>L peri-Sylvian-parietal infarct</td>
</tr>
<tr>
<td>38</td>
<td>8.5 days</td>
<td>R hemiplegia</td>
<td>Entire L MCA territory infarct</td>
</tr>
<tr>
<td>9</td>
<td>7 hours</td>
<td>Global aphasia</td>
<td>Extensive L MCA territory infarct with secondary hemorrhage</td>
</tr>
<tr>
<td>4</td>
<td>4 days</td>
<td>R h. hemianopia</td>
<td>R internal capsular infarct</td>
</tr>
<tr>
<td>30</td>
<td>3 days</td>
<td>R hemiparesis</td>
<td>Extensive L ACA and MCA territories infarct</td>
</tr>
<tr>
<td>13</td>
<td>1 day</td>
<td>Global aphasia</td>
<td>L peri-Sylvian-parietal infarct</td>
</tr>
<tr>
<td>7</td>
<td>7 days</td>
<td>R h. hemianopia</td>
<td>R hemiparesis</td>
</tr>
<tr>
<td>14</td>
<td>7 hours</td>
<td>Global aphasia</td>
<td>Entire L MCA territory infarct</td>
</tr>
<tr>
<td>16</td>
<td>2 days</td>
<td>Non-fluent dysphasia</td>
<td>Extensive L MCA territory infarct</td>
</tr>
<tr>
<td>7</td>
<td>7 days</td>
<td>R h. hemianopia</td>
<td>R hemiplegia</td>
</tr>
<tr>
<td>31</td>
<td>31 days</td>
<td>R facio-brachial plegia</td>
<td>R internal capsular infarct</td>
</tr>
<tr>
<td>18</td>
<td>1 day</td>
<td>L hemiparesis</td>
<td>Extensive L MCA territory infarct</td>
</tr>
<tr>
<td>7</td>
<td>7 days</td>
<td>R h. hemianopia</td>
<td>Extensive R MCA territory infarct</td>
</tr>
<tr>
<td>19</td>
<td>4.5 days</td>
<td>Global aphasia</td>
<td>L peri-Sylvian-parietal infarct</td>
</tr>
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<td>20</td>
<td>3 days</td>
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<td>R facial weakness</td>
</tr>
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<td>17</td>
<td>17 days</td>
<td>L facio-brachial plegia</td>
<td>R facial weakness</td>
</tr>
<tr>
<td>21</td>
<td>1.5 days</td>
<td>Non-fluent dysphasia</td>
<td>R facial weakness</td>
</tr>
</tbody>
</table>

L = left; R = right; h. = homonymous; ACA = anterior cerebral artery; MCA = middle cerebral artery.

*Studies on patient nos. 1, 3, 6, 8, 10, 11, 12, 15, 17, 26 and 35 not included, either because the studies were non-quantitative or because there was evidence of previous infarction in middle cerebral artery territory in the contralateral hemisphere (see text).

†First PET study done during the recovery phase of a left cerebral hemisphere transient ischemic attack, ten days before the onset of major stroke.

Infarct extended between the first and second PET studies.

Factors that may have influenced rO₂Av but not rCMRO₂ include arterial carbon dioxide tension (PaCO₂), systemic blood pressure (BP) and intracranial pressure (through their effects on CBF), and CaO₂. PaCO₂ amongst the forty-four studies had a wide range, 28.5–43.0 mm Hg. Contralateral 'cortical' CBF plotted against PaCO₂ showed a significant linear positive correlation (rCBF = −2.12 + 1.00 PaCO₂; r = 0.50; p < 0.001, by two-tailed t test) (fig. 2a). A linear negative correlation was found when 'cortical' OER was plotted against PaCO₂ (rOER = 0.97 − 0.014 PaCO₂; r = −0.57; p < 0.001, by two-tailed t test)† (fig. 2b). rCMRO₂ did not correlate with PaCO₂ (r = 0.04) (fig. 2c). Therefore, variable PaCO₂ between patients may have accounted, in part, for the inverse relationship between rOER and rO₂Av apparent in figure 1. No simple relationship between contralateral hemispheric CBF and BP or CaO₂ was found, and intracranial pressures were unknown. However, influences of these variables were evident in some studies. For example, patient no. 27 was anemic with low CaO₂, and contralateral CBF in this study was relatively high. Patient no. 28 died shortly after the PET study from raised intracranial pressure with trans-tentorial herniation (confirmed at post mortem), and contralateral CBF was the lowest of the series.

Whatever factors influencing rO₂Av were involved, figure 1 demonstrates that change in fractional oxygen extraction offset, at least in part, the variable oxygen supply in the contralateral hemispheres. This resulted in a poor linear correlation between rCMRO₂ and rCBF (r = 0.30)‡, with furthermore an increasing variation in rCMRO₂ at higher values of rCBF (fig. 3). In this series, if rCMRO₂ in the contralateral hemispheres had been predicted from measurements of rCBF alone, on the assumption that variations of the former were associated with similar percentage changes in the latter, errors of up to 160% would have resulted.

‡Mean measured rCBV-correction of rCMRO₂ in thirty-three studies was 10 ± 4%. If a correction of 10% was applied to the eleven uncorrected rCMRO₂ values, r = 0.27.
TABLE 1 (continued)

<table>
<thead>
<tr>
<th>Patient No.*</th>
<th>Timing of PET scans from ictus</th>
<th>Presenting signs</th>
<th>X-ray CT scan appearances</th>
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<tr>
<td>22 - 10 days†</td>
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<tr>
<td>7 hours</td>
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<td>4 days</td>
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<td></td>
</tr>
<tr>
<td>23</td>
<td>2.5 days‡</td>
<td></td>
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<tr>
<td>7 days</td>
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<td></td>
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<tr>
<td>24</td>
<td>1.5 days</td>
<td></td>
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<tr>
<td>4 days</td>
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<td>17 days</td>
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<td>6 days</td>
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<td></td>
</tr>
<tr>
<td>27</td>
<td>1.5 hours</td>
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<tr>
<td>7 days</td>
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<td>28</td>
<td>4.5 days</td>
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<td>29</td>
<td>8 hours</td>
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<td>3 days</td>
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<td>1 day</td>
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</tr>
<tr>
<td>31</td>
<td>1.5 years</td>
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<tr>
<td>32</td>
<td>8 days</td>
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<tr>
<td>33</td>
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</tr>
<tr>
<td>36</td>
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<td></td>
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</table>

It is common practice to correct CBF measurements for PaCO2. The slope of figure 2a (1 ml/100 ml/min per 1 mm Hg) was used to correct individual rCBF measurements to PaCO2 = 40 mm Hg. The linear correlation between "PaCO2-corrected" rCBF and rCMRO2 was also poor (r = 0.31). Moreover, such an overall correction is of dubious validity, as is considered further in the discussion.

Contralateral 'cortical' CMRO2 was analysed to judge whether there was metabolic evidence of diaschisis. One study for each of the twenty-five stroke patients was selected. As Slater et al5 have reported that contralateral hemispheric CBF is lowest several days after the ictus, a study between twenty-four hours and seven days after the ictus was chosen if there was more than one study on an individual patient. Mean interval from the ictus for these 25 studies was 2.7 ± 1.9 days (range seven hours to eight days). 'Cortical' CMRO2 was 12% lower than normal contralateral to cerebral infarcts, but a similar reduction was also observed in the patients with extracranial cerebrovascular disease without previous overt infarction (table 4). An analysis of variance was performed on the data, once it has been established by the Kolmogorov-Smirnov one-sample test and by Bartlett's test that the within level distributions were normal and that the residual variance was similar in the three groups. The anovar demonstrated a difference among the means of the groups. Detailed comparisons by F-tests showed that rCMRO2, contralateral to infarct was different from normal with a significance at the 1% level — a statistically significant difference by the Bonferroni method. It was not different from mean rCMRO2 in patients with vascular disease without previous infarction. Mean rOER in this last group of patients (0.45 ± 0.04) demonstrated that oxygen supply was not limiting, that is the reduction of 'cortical' CMRO2 in these patients was not the result of chronic ischemia (previous studies have shown a rise in rOER up to 0.90 or greater in response to ischemia15).

Contralateral rCMRO2 did not correlate with the size of the infarct in the other hemisphere. Mean contralateral rCMRO2 in the eight studies on the seven patients with small white matter infarcts was 2.9 ± 0.4 ml/100 ml/min (measured rCBV-correction in four, estimated in the other four), and it was 2.8 ± 0.3 ml/100 ml/min in the twenty-seven studies on the fourteen patients with extensive middle cerebral artery territory infarction (measured rCBV-correction in twenty, estimated in the other seven).

There was no correlation between contralateral rCMRO2 and time after the onset of stroke, and no
TABLE 3

Comparison between the Patient and Two Control Groups (mean values ± standard deviation)

<table>
<thead>
<tr>
<th>No. of studies</th>
<th>Stroke patients</th>
<th>Normal controls</th>
<th>Vascular controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>63 ± 15</td>
<td>50 ± 15</td>
<td>61 ± 19</td>
</tr>
<tr>
<td>Age range (years)</td>
<td>23-87</td>
<td>22-73</td>
<td>47-72</td>
</tr>
<tr>
<td>Sex</td>
<td>15 M:10 F</td>
<td>12 M:6 F</td>
<td>7 M:3 F</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>145 ± 25</td>
<td>130 ± 25</td>
<td>160 ± 25</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>80 ± 10</td>
<td>75 ± 5</td>
<td>95 ± 15</td>
</tr>
<tr>
<td>PaCO₂ (mm Hg)</td>
<td>36.2 ± 3.3</td>
<td>40.8 ± 2.7</td>
<td>39.6 ± 2.2</td>
</tr>
<tr>
<td>CaO₂ (ml/100 ml)</td>
<td>19.3 ± 2.3</td>
<td>18.1 ± 1.9</td>
<td>17.7 ± 1.9</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>14.2 ± 1.8</td>
<td>13.3 ± 1.4</td>
<td>13.0 ± 1.4</td>
</tr>
</tbody>
</table>

BP = blood pressure; PaCO₂ = arterial carbon dioxide tension; CaO₂ = arterial oxygen content; M = male; F = female.

A reciprocal relationship between rCBF and rOER was observed in this series in relation to the individual variations in PaCO₂. The positive correlation between rCBF and PaCO₂, and the negative correlation between rOER and PaCO₂, reflected the independence of rCMRO₂ from PaCO₂. Although variable PaCO₂ was a recognisable influence on oxygen supply, it was likely that other factors were important in individual studies. The net result was a wide range of values for the rate of supply of oxygen to the contralateral hemispheres. The negative correlation between rOER and O₂Av demonstrated that this variability in oxygen supply was not the consequence of an equally wide range of rCMRO₂. It was, therefore, not unexpected that rCBF and rCMRO₂ did not correlate, a reflection of the uncontrolled nature of observations on human subjects. Good correlation between rCBF and rCMRO₂ could only be anticipated if the diverse physiological variables that influence rCBF independently of rCMRO₂ were, fortuitously, relatively constant amongst the individuals in a series. In the light of the results presented...
FIGURE 2. a) Cerebral blood flow (CBF) in the cortex of the contralateral hemispheres plotted against arterial carbon dioxide tensions (PaCO₂). Linear regression analysis demonstrated a significant positive correlation. b) Fractional oxygen extraction (OER) in the cortex of the contralateral hemispheres plotted against PaCO₂. There was a significant negative correlation. c) Oxygen consumption (CMRO₂) in the cortex of the contralateral hemispheres plotted against PaCO₂. The influence of PaCO₂ on CBF was offset by opposite change in rOER, and rCMRO₂ was independent of PaCO₂. (Closed circles, rOER and rCMRO₂ data rCBV-corrected; open circles, rOER and rCMRO₂ data not corrected for rCBV. Inclusion of uncorrected data made little difference to the correlations — see text).

FIGURE 3. Oxygen consumption (CMRO₂) in the cortex of the contralateral hemispheres plotted against cerebral blood flow (CBF). (Closed circles, rCMRO₂ data rCBV-corrected; open circles, rCMRO₂ data not corrected for rCBV).

TABLE 4 Comparison of "Cortical" CMRO₂ in Normal Controls, in the Hemispheres Contralateral to Recent Middle Cerebral Artery Territory Infarcts, and in Patients with Extracranial Vascular Disease but Without Cerebral Infarction (mean values ± standard deviation)

<table>
<thead>
<tr>
<th></th>
<th>Normals</th>
<th>Contralateral to infarcts</th>
<th>Vascular disease without infarction</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>17*</td>
<td>25*</td>
<td>10*</td>
</tr>
<tr>
<td>rCMRO₂ (ml/100 ml/min)</td>
<td>3.3 ± 0.4</td>
<td>2.9 ± 0.4</td>
<td>2.9 ± 0.5</td>
</tr>
</tbody>
</table>

*In group A, there was measured rCBV-correction of rCMRO₂ in 7 studies estimated rCBV-correction in the other 10; in group B, 19 and 6 studies, respectively; and in group C, all studies had measured rCBV-correction of rCMRO₂.

Results of analysis of variance

Source of variation         Variance ratio (F)  
A v. B v. C                  5.781

Detailed comparisons

A v. B                       9.771
A v. C                       7.051
B v. C                       0.04

†Significant at the 5% level; ‡significant at the 1% level. According to the Bonferroni method, the detailed comparisons can only be considered significant at the 1% level or less.
reactivity — this may partly explain why the correlation between rCBF and PaCO2 in figure 2a was far from perfect. Therefore, it cannot be assumed that this overall correlation would result in a reasonable approximation for individual corrections of rCBF for PaCO2. The poor correlation between "PaCO2-corrected" rCBF and rCMRO2 in the contratralateral hemispheres, using the mean correction, may reflect this inaccuracy as much as the possible influence of factors other than variable PaCO2 on rCBF.

The rate of oxidative metabolism in the contratralateral hemispheres was lower than normal, apparently confirming the presence of transhemispheric diaschisis. However, the subjects with extracranial cerebrovascular disease but without evidence of previous cerebral infarction had a mean 'cortical' CMRO2 no different from the hemispheres contratralateral to recent infarcts. There was no evidence of chronic ischemia in these patients with carotid artery occlusion as mean rOER was not increased (and, therefore, metabolism was not limited by oxygen supply). Why mean 'cortical' CMRO2 was lower in this group is a matter for speculation, but if any of these patients had had a stroke, comparison of contratralateral CMRO2 with normal controls to 'demonstrate' diaschisis would have been very misleading. It then becomes impossible to say whether low rCMRO2 in the hemisphere contratralateral to an infarct is the result of diaschisis or preceded the stroke, unless the individual had fortuitously also been studied prior to the stroke.

In all other reports of diaschisis it has been tacitly assumed that chronic hypertension, diabetes, extracranial vascular disease, etc., variably present in the patients studied and predisposing to their strokes, had no influence on rCMRO2, prior to the onset of cerebral infarction. In this series the patients at risk from stroke were obviously a highly selected group, and they had not been matched to the stroke patients in terms of the degree of carotid atheromatous occlusive disease — this was not possible, as few of the stroke patients underwent arteriography (an investigation not usually considered necessary on clinical grounds in such circumstances, at least in the United Kingdom). Therefore, this study does not prove that transhemispheric diaschisis does not occur, but it demonstrates that such diaschisis has not been established in human studies because of the use of inappropriate controls, that is subjects free of chronic diseases predisposing to stroke. This conclusion receives further support from the observation that contratralateral rCMRO2 was the same with small white matter infarcts as it was in association with very extensive hemispheric damage. Intuitively, it seems unlikely that the degree of diaschisis would not be dependent on the extent of cerebral injury.

One obvious reservation about this study is that the lack of systematic serial studies may have masked a transient metabolic depression only present for a few days after the ictus, as suggested in a previous study. However, as an extension of this argument, the only method that will unequivocally demonstrate whether transhemispheric diaschisis occurs to any appreciable degree in man is to perform observations on a group of patients at high risk of stroke, so that if cerebral infarction subsequently occurs the individual has acted as his own control.

Acknowledgments
The authors thank Mr D D Vonberg, Director, and the many other members of the MRC Cyclotron Unit for their invaluable support, especially Mr P D Buckingham and the members of the Radiochemistry Section.

References
FROM CLINICAL EXPERIENCE it is well known that patients with acute stroke, even without a history of previous hypertension, often have a very high blood pressure (BP) on arrival at hospital. Mechanisms and effects of the BP elevation are unclear. Is the BP response harmful to the brain by increasing the tendency of blood-brain barrier disruption and edema formation? Or is it a beneficial response to increased demands of perfusion? The Joint Committee for Stroke has concluded that extremely high BP levels should be treated, but no limits are given. WHO has recommended cautious therapy in patients with extreme hypertension, such therapy is not evaluated. If this is to be done, the present findings have to be taken into consideration. Stroke controls, matched according to the initial BP level, will thus be required.

NO EVIDENCE FOR DIASCHISIS/Wise et al

Blood Pressure Course In Patients With Acute Stroke and Matched Controls
M. Britton, M.D., A. Carlsson, M.D., and U. de Faire, M.D.

SUMMARY The natural course of blood pressure (BP) was studied after emergency hospitalization in 209 consecutive stroke patients and as many age and sex matched controls. Histories of hypertension were more common among patients than controls (46% vs 26%). On admission 69% of the stroke group and 36% of the controls had BP ≥ 170/100 mm Hg. In the first four days there was a spontaneous BP decline, which was greater the higher the initial values. During the whole hospitalization though, stroke patients with previous hypertension had the highest BP levels and previously normotensive controls the lowest.

Even if WHO as well as the Joint Committee for Stroke have recommended cautious antihypertensive therapy in stroke patients with extreme hypertension, such therapy is not evaluated. If this is to be done, the present findings have to be taken into consideration. Stroke controls, matched according to the initial BP level, will thus be required.

The question of treatment must be answered in the light of knowledge about the spontaneous BP course. Wallace et al found a gradual decrease of BP in 334 stroke patients referred to them for treatment. Our aim was to study consecutive, nonselected patients and to evaluate whether the BP reaction was specific for stroke patients. Or was it merely a common response to acute disease and hospitalization in elderly subjects? A comparison was therefore made with age and sex-matched controls admitted for acute disorders other than stroke.

Material and Methods
Included in this study were 209 patients consecutively admitted to the Stroke Unit at the Medical Department of Serafimer Hospital in Stockholm. The hospital served all inhabitants in a defined area of Stockholm and the unit admitted a representative part of the stroke cases. In the group studied were 113 men (mean age 71, range 50–94 years) and 96 women (mean age 76, range 50–96 years).

As admission criteria, acute onset of focal neurological deficit was required. Attacks of vertigo or syncope without focal neurological deficit were not included. In addition to fulfillment of the admission criteria, the following diagnostic definitions were used: cerebral hemorrhage — hemorrhagic cerebrospinal fluid (CSF) or intracerebral hemorrhage at CT scan; atherothrombotic brain infarction — bleeding had been excluded with CSF analyses or CT scan; cerebral embolus — the same as for atherothrombotic
No evidence for transhemispheric diaschisis after human cerebral infarction.
R Wise, J Gibbs, R Frackowiak, J Marshall and T Jones

Stroke. 1986;17:853-861
doi: 10.1161/01.STR.17.5.853

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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