Compartamental analysis of regional cerebral blood flow in patients with acute severe head injuries

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Bicompartmental analysis for the calculation of regional cerebral blood flow (rCBF) from 133Xe clearance in brain tissue has not been thoroughly explored in clinical studies. Most authors rely either on the average rCBF obtained by height/area analysis of the clearance curves or on the initial-slope flow index. Possibly the reason is that the validity of the bimodal flow distribution in abnormal brain tissue is considered questionable. In the present study, bicompartmental analysis, performed by a least-square computerized iterative approach, was used in the calculation of the flow and weight of the tissue of the brain of patients with severe head injuries. The analysis was found to give important information of the nature and course of the brain lesions even if the clearance curves did not have the normal bi-exponential shape, provided the results obtained were properly interpreted. In such cases, the values of the flow and relative weight could not be taken as flow and weight values of gray and white matter, but rather as indices of fast and slower flow components. The interpretation of the results was based on the identification of three types of 13-minute clearance curves, each being characteristic of a type of brain lesion. The clearance curves from fairly normal brain tissue appeared to be bi-exponential; curves from areas of severe cortical contusion had, in addition, an initial and rapid "third" component, a tissue peak, whereas curves from severely edematous brain tissue approached the mono-exponential shape.

KEY WORDS  •  severe head injury  •  regional cerebral blood flow  •  compartmental analysis

The clearance of inert, freely diffusible tracers from the brain tissue is frequently described by a bicompartamental model; one compartment (the fast one) representing the gray matter, the other (the slow one) representing the white matter. In normal human brain tissue at normocapnia and in some pathological conditions of degenerative brain disease, the bicompartamental model reflects fairly well the average values of flow and weight for the gray and white matter, but in abnormal brain tissue, when the blood flow is abnormally high, as in hyperemia, or abnormally low, as in ischemia and brain edema, this bimodal flow distribution does not fit. Several authors have stated that, under these circumstances, the relative contribution of the two compartments does not reflect the anatomical classification in gray and white matter, but rather the relative contribution of rapidly and less rapidly perfused compartments without regard to the anatomical constitution. Moreover, as some authors have found that...
an initial and fast "third" component (a tissue peak) can occur in the clearance curves from areas of abnormal brain tissue, it may be questioned if the bimodal method of calculation is justified in abnormal brain tissue.

In the study presented here we have used the bicompartamental model in the calculation of flow conditions in a group of patients with severe head injuries, although we knew from initial-slope flow-index calculation that very low flow, abnormally high flow, as well as tissue peaks were common in these patients. Material and methods have been described in previous papers. Only a summary will be given here.

Clinical Materials and Methods

Patient Selection

Twenty-three patients ranging in age from 14 to 70 (average 28.3) years were studied during the acute phase lasting 3 to 21 days after a severe head injury. On admission, all were deeply comatose and only patients who, after the initial neurosurgical treatment, were still deeply comatose were included in the series. Emergency management included intubation with controlled respiration, carotid angiography, and craniotomy (17 cases), or exploratory burr holes (four cases). The severity of the cortical lesions (contusion, laceration, and edema) were carefully assessed. In only two patients was the cortex not inspected initially. Both had brain-stem symptoms but no signs of cortical lesions, and normal angiography. All patients were treated with artificial ventilation, and the study was concluded when the respirator treatment was stopped. The ventilation was maintained with positive pressure and controlled respiration, and the \( PaCO_2 \) and \( PaO_2 \) were maintained at levels of 20 to 40 mm Hg and 100 to 150 mm Hg, respectively. The cerebral intraventricular pressure (IVP) was measured continuously during the entire study by the method of Lundberg. The basic pressure was kept below 45 mm Hg by means of administration of meperidine, chlorpromazine, hyperventilation, manitol, Nembutal (pentobarbital), Pentothal (thiopental) dexamethasone, ventricular drainage, and, as a last resort, surgical decompression.

Based on the clinical picture, carotid angiography, and the operative findings, the patients were divided into three groups:

Group I: Patients with Cerebral Cortical Lesions. Six patients on admission were comatose with purposive flexor movements on pain. They all had focal neurological deficits in the form of hemiparesis and/or abnormal reflexes of the extremities on the side contralateral to the cortical lesion, but they had never had attacks of decerebrate rigidity or abnormal brain-stem reflexes. The carotid angiography carried out on admission showed signs of a localized mass lesion, and craniotomy disclosed severe contusion and laceration with hematoma.

Group II: Patients with Brain-Stem Symptoms. This group consisted of five patients who on admission were comatose and reacted to pain with extensor movements. All five had attacks of decerebrate rigidity and abnormal brain-stem reflexes from the very beginning, but no focal cortical deficits. In all five patients, the carotid angiography carried out on admission was normal. In three of the patients, the cerebral cortex was explored bilaterally through burr holes, and found to be normal. In the remaining two patients, exploration was not considered to be indicated.

Group III: Patients with Cerebral Cortical Lesions and Brain-Stem Symptoms. This group included 12 patients who were all comatose on admission. Nine had extensor movements on pain and attacks of decerebrate rigidity, and eight had also shown abnormal brain-stem reflexes from the very beginning. Two patients reacted to pain with purposive flexor movements on admission, but they had attacks of decerebrate rigidity and abnormal brain-stem reflexes 4 days after the injury in association with high IVP (basic pressure about 45 mm Hg and multiple plateau waves of 30 minutes' duration). One patient showed no motor reaction at all from admission until he died 3 days after the injury. In all cases, the carotid angiograms showed signs of a localized mass lesion. In 11 of the patients, the cortical lesions were assessed through craniotomy, and in one, through enlarged burr holes. In all twelve, severe cortical contusion and a varying degree of edema were found. In seven, laceration with hematoma was also present.

In four patients, high IVP (basic pressure about 45 mm Hg and multiple plateau waves) indicated a new angiography 6 to 8 days after the injury, and in three the angiograms
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revealed signs of a mass lesion in the most injured hemisphere. All three patients underwent renewed craniotomy, which in one of them disclosed a small hematoma (20 ml). In the remaining two, only severe edema was found in the area of the mass lesion.

Methods

The regional cerebral blood flow was measured repeatedly in each patient during the first 18 days after the trauma, using the intra-carotid $^{133}$Xe injection technique. The time interval between the individual cerebral blood flow (CBF) studies depended on the indications for carotid angiography, and the CBF measurement was always done before the angiography. A total of 203 CBF runs were made in 66 separate CBF studies, producing 3248 $^{133}$Xe clearance curves. The clearance of the isotope was recorded for 15 minutes by 16 NaI scintillation detectors placed extracranially over the area to be studied. The counts were simultaneously stored on a 16-track magnetic tape, and after the measurement, transferred to a punch tape from which they could be used for electronic data processing. The data were analyzed on a CDC-6400 computer with a program developed by one of us (F.T.J.). Simultaneously with the punching, the logarithmic clearance curves were written out, and the shape and quality of the curves were assessed.

During the CBF determinations, the pressure in the internal carotid artery, systemic arterial blood pressure (SAP), was measured through the carotid catheter, and the IVP was measured through a catheter inserted into one of the lateral ventricles of the brain. Both pressures were measured continuously and simultaneously recorded by Statham P37 transducers and a Hokushin 2-channel writer, and expressed as mean pressures (diastolic + 1/3 pulse pressure) in terms of mm Hg. The mean perfusion pressure was calculated as SAP minus IVP.

At the start of each CBF determination, samples of blood were drawn from the carotid artery for determination of arterial pCO$_2$, pO$_2$, pH, and hemoglobin.

The cerebral autoregulation was tested repeatedly in 21 of the patients by infusion of angiotensin, showing a blood pressure rise of 20% to 40%. The cerebrovascular reactivity was tested repeatedly in 14 patients by means of a hyperventilation test, showing a decrease in PaCO$_2$ of 5 to 10 mm Hg.

All CBF studies were performed under local anesthesia, and before the determinations the patients were given meperidine, chlorpromazine, and pancuronium bromide, the same sedatives as they were receiving on the ward. In addition, they had a single dose of atropine. The CBF measurements were never performed within the first 6 hours after a neurosurgical intervention and at the earliest 12 hours after the injury.

Calculations

The calculations were made by computer according to Høedt-Rasmussen, et al., and Ingvar, et al. The computer calculated the flow and relative weights of the fast (Fr, Wf) and slow (Fs, Ws) compartments of the brain tissue by compartmental analyses of the first 13 minutes of the clearance curves. The flow parameters were calculated, using a least-squares iterative approach. The computer started the procedure of calculation when the activity had decreased for 15 seconds (three successive data points) and when the decrease in activity was less than 5 standard deviations. This starting procedure excluded shunt peaks and plateaus from the calculation.

The equation of the bi-exponential clearance curves was

\[ Y = A \times \exp(-\alpha t) + B \times \exp(-\beta t) \]

where \( Y \) is the theoretical value of the bi-exponential model, \( A \) and \( B \) are intercepts, and \( \alpha \) and \( \beta \) are rate constants. The parameters of the non-linearized model were estimated by a weighted least-squares principle. The iteration was carried out until the \( \Delta \alpha \) and \( \Delta \beta \) were less than 1% of \( \alpha \) and \( \beta \), respectively.

The partition coefficients were those used for normal gray and white matter, respectively, corrected to the present hemoglobin concentration.

The relative weights \( W_f \) and \( W_s \) were calculated according to Høedt-Rasmussen by the equations:

\[
W_s = \frac{I_s \times F_s/F_s}{I_s \times F_s/F_s + I_f} \times 100,
\]

\[
W_f = 100 - W_s,
\]

where \( W_f \) and \( W_s \) are the relative weights of
the fast and slow compartments, respectively, and \( I_f \) and \( I_s \) the intercepts. The residual activity was measured during the last 1 minute before the CBF measurements were made, and considered to be cleared in the white matter, and then used to correct the white matter intercept. The flow values were calculated as \( \text{ml}/100 \text{ gm/min} \) and the relative weights as percentages.

As a test for the accuracy of the curve fitting, the computer calculated the weighted conditioned variance (VAR.ERR.)\(^4\) as follows:

\[
\text{VAR.ERR.} = \frac{\sum (y_i - \bar{y})^2}{\bar{y}_i}
\]

where \( n \) = degrees of freedom. The VAR.ERR., which was used as a testor, is a \( C^2 \) (chi-square/\( n - 1 \)) variable and the critical values were found to be: 0.784 < VAR.ERR. < 1.242 (\( p \leq 0.05 \)).

In addition, the computer calculated CBF\(_{10}\) (\( F_{10} \)) by the height/area formula; and the initial-slope flow index \( F_1 \).

\[
\text{CBF}_{10} = \frac{H_{\text{max}} - H_{10}}{A_{10}} \times \lambda_{\text{brain}} \times 100
\]

\[
\text{ml}/100 \text{ gm/min}
\]

where \( H_{\text{max}} \) is the maximal counting rate, \( H_{10} \) the counting rate at 10 minutes, \( A_{10} \) the summation of the tissue concentration, and \( \lambda_{\text{brain}} \) the brain/blood partition coefficient for normal brain homogenates corrected to the present hemoglobin concentration.

\[
F_1 = k \times \lambda_{\text{gray}} \times 100 \text{ (ml}/100 \text{ gm/min})
\]

where \( k \) is the rate constant of \(^{133}\text{Xe}\) in the first minute of the clearance, and \( \lambda_{\text{gray}} \) the brain/blood partition coefficient for normal gray matter,\(^6\) at the present hemoglobin concentration.

**Results**

Comparisons between the cortical lesions in each area, as assessed at the neurosurgical operations, the shape of the clearance curves and the regional flow values resulted in the following conclusions. The abbreviations \( rF_f \), \( rW_f \), and \( rF_s \), \( rW_s \) denote flow and relative weight values of the regional fast and slow compartments, respectively, regardless of the anatomical constitution.

**Fairly Normal Brain Tissue**

In areas that were described as being of fairly normal appearance at the neurosurgical craniotomy, the flow curves appeared to be bi-exponential (Fig. 1 A), and the bi-exponential model fitted very well to the clearance curves, the VAR.ERR. being within the 5% limit (Fig. 2 upper). Both the \( rF_f \) and \( rW_f \) values were slightly to moderately reduced. However, \( rF_f \) was rarely below 40 ml/100 gm/min, and \( rW_f \) rarely below 40%. Such "bi-exponential" 13-minute clearance curves were found over the whole hemisphere in patients with brain-stem lesions unaccompanied by severe cortical lesions and severe edema, and in patients with cortical lesions in noncontused and in moderately contused areas of the cortex.

The reaction to induced hypertension was either unchanged flow conditions (preserved autoregulation) or an increase in \( rF_f \) without any appreciable change in \( rW_f \) (impaired autoregulation).

The reaction to hyperventilation was most frequently a fall in \( rF_f \) without any appreciable change in \( rW_f \) (normal reaction). In some cases in which the mean flow values, \( \text{rCBF}_{10} \), became very low (below 30 ml/100 gm/min) during hyperventilation, the clearance curves changed and became almost mono-exponential of appearance. In these cases, a considerable increase in \( rF_f \) occurred, accompanied by a steep fall in \( rW_f \).

Figure 3 shows the flow conditions in a 23-year-old man with moderate cortical contusion. On admission, he had an epidural hematoma (60 ml), but only slight contusion in the parietal regions of the right hemisphere (shaded area). The CBF was measured 15 hours after the trauma (8 hours after the operation at which the epidural hematoma was removed).

**Contused Brain Tissue**

In areas of severe cortical contusion but without pronounced edema, the clearance curves were found to be of abnormal appearance (Fig. 1 B). The bi-exponential model fitted poorly to the clearance curves, the VAR.ERR. being outside the 5% limit (Fig. 2 lower) as they had a rapid "third" component initially, corresponding to a tissue peak.\(^4,6\) In these areas, the bicompartimentally calculated \( rF_f \) values were high (as compared...
with those outside the contusion), and the $rW_r$ values were reduced, although rarely below 20%. Such "three-exponential" 13-minute clearance curves were found in patients with cortical laceration or contusion, and only in severely contused areas. It was a characteristic feature that the most contused areas had the highest weight of the fast compartments ($rW_f$), corresponding with the most marked tissue peaks (Figs. 4 and 6). On improvement in the patient's clinical condition, the clearance curves lost the rapid "third" component; $rF_f$ fell to subnormal levels, $rW_r$ approached normal values, and the curve fitting became good.

During autoregulation tests the clearance curves either remained unchanged (preserved autoregulation?) in the central part of the contusion (the tissue peak areas) or the peaks became more marked ($rW_f$ increased), while tissue peaks occurred in the peripheral part of the contusion, resulting in an increase in $rF_f$ but a decrease in $rW_r$. Both reactions may presumably be interpreted as signs of impaired autoregulation.

During hyperventilation the tissue peaks became less pronounced, and the clearance curve appeared more bi-exponential and $rF_f$ decreased, whereas $rW_r$ increased.

Figure 4 shows the flow conditions in a 66-year-old man with severe contusion without pronounced edema. On admission, he had a subdural hematoma (250 ml), and severe contusion in the frontal and temporal regions (shaded area) of the left hemisphere. Lacerations were seen in the frontal and temporal poles. The hematoma was removed at the initial operation. Neither the IVP (12 mm Hg), nor the carotid angiography following the CBF measurement gave rise to suspicion of severe edema. The CBF determination was made 34 hours after the injury.

From the sixth day after the trauma, IVP increased to a maximum value of 50 mm Hg. The CBF was measured again on the seventh day (Fig. 7). Carotid angiography following that CBF measurement gave rise to suspicion of severe edema. The CBF determination was made 34 hours after the injury.

Edematous Brain Tissue

In areas with pronounced cerebral edema but without evidence of significant contusion, we found 13-minute curves of almost mono-exponential appearance (Fig. 1 C) and the curve fitting suffered but was still acceptable. In these areas, the $rF_f$ values were high, most frequently above the normal level of flow in the gray matter ($rF_g$), 80 ml/100 gm/min, and the $rW_r$ values were below 20%. The mean flow values were low, the $rCBF_{10}$ being between 20 and 30 ml/100 gm/min. Such
FIG. 2. Upper: Linear transcription of a clearance curve from fairly normal brain tissue. Note the perfect fitting of the observed data with the calculated curve. The VAR.ERR. is within the 5% limit.
Fig. 2. Lower: Linear transcription of a clearance curve from severely contused brain tissue. Note the poor fitting in the initial part of the curve. At the starting point, the counts of the calculated curve are 13% lower than the observed counts. The VAR.ERR. is outside the 5% limit.
FIG. 3. Semi-logarithmic 13-minute clearance curves (A), rFt values (B), and rWt values (C) from "normal" brain tissue. The flow curves appear bi-exponential. The rFt and rWt values are somewhat decreased. The rFt values are a little higher and the rWt a little lower in the moderately contused (shaded) areas than in the remaining brain tissue.

FIG. 4. Semi-logarithmic 13-minute clearance curves (A), rFt values (B), and rWt values (C) from severely contused brain tissue. It is seen that the flow curves from the frontal and temporal regions have a steep part initially, a rapid "third" component. The rFt values are higher and the rWt values a little lower in the contused (shaded) areas than in the rest of the hemisphere. In the contused areas the rWt values are highest in the temporal region where the third components (the tissue peaks) are most marked and the contusion most severe.
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Fig. 5. Semi-logarithmic 13-minute clearance curves (A), rFr (B), and rWt (C) from edematous brain tissue. The clearance curves are almost mono-exponential of appearance. The rFr values are high and the rWt values very low, especially in the temporal regions, where the edema was most pronounced (shaded area).

"Mono-exponential" clearance curves were found in patients with elevated IVP; namely, in one patient with brain-stem symptoms and very high IVP, but without focal cortical lesions, and in five patients with cortical lesions accompanied by pronounced edema, appearing as a mass lesion in the angiograms. In the latter, the curves outside the areas of severe cortical contusion appeared "mono-exponential." In four of the five patients, the cortical lesions (contusion, edema) were verified during operation (three cases) or autopsy (one case).

The autoregulation response varied. Sometimes the angiotensin infusion did not change the clearance curves and the flow parameters (preserved autoregulation), but usually a change in the 13-minute clearance curves was seen. They appeared more bi-exponential, and the rFr values decreased, whereas the rWt values increased simultaneously with an increase in the rCBF values (impaired autoregulation).

During hyperventilation, the clearance curves became even more mono-exponential in appearance, and the rFr values increased; the rWt values decreased, and the rCBF decreased (preserved hyperventilation response). Thus, preserved hyperventilation response appeared as a decrease in the relative weight of the fast compartment.

Figure 5 shows the flow condition in a 53-year-old man with pronounced edema of the brain tissue, most in the temporal region. On admission, he had a subdural hematoma and contusion in the lower temporal region (shaded area) on the left side of the brain. The hematoma (30 ml) was removed at the initial neurosurgical operation. During the first 24 hours the IVP was about 20 mm Hg, and the carotid angiograms taken 24 hours after the admission revealed signs of edema in the left hemisphere, especially in the temporal region. The anterior cerebral artery and the internal cerebral vein were displaced 5 mm to the right, and the vessels in the temporal region were stretched and displaced. The CBF measurements were made on the left side 23 hours after the head injury, just before angiography.

In this case, the rWt was below 20% in spite of some contusion of the tissue. This was an exception and indicated that the contusion in the areas where the CBF was measured may...
not be severe. In agreement with this observation, autopsy performed 3 weeks later showed severe contusion of the base of the brain, whereas the lateral aspect of the brain was less contused.

Contused and Edematous Brain Tissue

In areas in which the craniotomy disclosed both severe contusion and severe edema, the flow conditions were more difficult to assess, as increasing edema in the contused areas suppressed the rapid third flow component. In the patients with severe cortical contusion and increasing IVP, indicating increasing edema, the clearance curves gradually approached the “mono-exponential” appearance, and an increase in rFr accompanied by a decrease in rWr occurred simultaneously with a decrease in rCBFio. Thus, the flow conditions in patients with cortical contusion and progressive edema gradually approached the flow conditions seen in patients with pronounced edema, but without contusion. However, only in a few areas with contusion (Fig. 5) did the rWr values decrease below 15%.

The flow conditions in a 14-year-old boy with severe cortical contusion and increasing edema are illustrated in Fig. 6. On admission, he had a subdural hematoma (30 ml) and severe contusion and edema in the frontal and temporal regions (shaded area) of the right hemisphere. At the initial craniotomy severe venous bleeding occurred; the blood pressure fell and was unobtainable for 3 to 5 minutes. Three days after the injury, clearance curves of the frontal and temporal regions had an initial rapid compartment, a tissue peak (Fig. 6 A and B). In these regions, the rFr values were high, but the rWr values were only slightly decreased. The IVP was 27 mm Hg. Five days after the injury, the IVP had in-
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creased to 35 mm Hg, and attacks of decerebrate rigidity had developed (Fig. 6 C and D). It is seen that the rWr values had decreased somewhat in the contused areas and the rFr had increased a little. In the less contused areas parietally, the rWr values had decreased below 35%, and the rFr had increased markedly. These results revealed the progress of the edema in severely contused brain tissue. Two days later numerous plateau waves of long duration had developed, and exploration of the temporal lobe was done. At the operation, massive edema of the temporal lobe was found, and temporal decompression and resection of the temporal pole were performed. Twelve days after the injury, the brain bulged through the temporal decompression as a sign of pronounced edema, but the IVP had decreased to 25 mm Hg, probably because of the decompression. The rCBFxo had decreased to very low values. In the contused and severely edematous areas in the temporal region (corresponding to the decompression) the rWr had further decreased. Outside these areas in the parietal and frontal regions the rWt had increased to near normal and rFr decreased to subnormal values, which corresponded to the low level of consciousness. These results revealed that the edema had increased in the area of the decompression, but decreased in the other areas of the hemisphere.

During induced hypertension, the findings were essentially the same as in edematous tissue: the clearance curves were unchanged (normal autoregulation?) or appeared more bi-exponential; the rFr decreased and the rWt increased, while the rCBFxo increased, indicating impaired autoregulation.

During hyperventilation, the mono-exponential appearance of the clearance curves increased in the most edematous brain tissue in the center of the contusion and rFr increased, whereas rWr decreased. In the periphery of the contusion, a fall in either the rFr or rWr occurred. In both cases, the rCBFxo values fell as a sign of hyperventilation responsiveness (Fig. 7).

Discussion

The use of the bicompartiment model in the calculation of blood flow in the gray and white matter requires that the brain tissue can be regarded as two well defined compartments representing gray and white matter, respectively. This requirement is, in all essentials, fulfilled in the study of normal or slightly pathological brain tissue at normocapnia, but in case of severely pathological brain tissue the use of the bicompartiment model is problematic. In a previous paper, we showed that the bi-exponential model fitted poorly to the clearance curves if the VAR.ERR. was situated outside the 5% limit (Fig. 2 lower).

In the present study we found that, in patients with severe head injuries, the 13-minute clearance curves did not appear bi-exponential when the tissue showed severe contusion or pronounced edema (Fig. 1 B and C), and the VAR.ERR. was in the case of severe contusion outside the 5% limit.

In areas with severe cortical contusion, the clearance curves had an initial and rapid “third” component, a tissue peak. The bicompartimental model fitted poorly, especially in the initial part of the clearance curves, and the calculated intercepts of the curves were consistently situated at least 8% to 13% lower than the observed intercepts (Fig. 2 lower). In spite of this underestimation, the rFr values for the severely contused areas were high, as compared with the flow values outside the contusions in the acute phase of head injuries. The rWr apparently varied with the degree of the edema in the tissue, as it decreased with increasing edema. However, the rWr rarely decreased below 20% in severely contused areas. Thus, high rFr indicated contusion if rWr was above 20% (see below). The calculated rFr and rWr were not true values, since the basis for the calculation, the bi-exponential model, did not fit.

In areas with pronounced edema, the 13-minute clearance curves approached the mono-exponential shape (Fig. 5), and the mean flow (rCBFxo) values were very low, usually below 30 ml/100 gm/min. In these areas, the compartmentally calculated rFr was high, but the rWr was usually below 20% and often below 10%. It is therefore likely that in severely edematous tissue, most of the flow in the gray matter has approached the flow values of the white matter to such an extent that a distinction between gray and white compartments cannot be made. The calculated rFr may either consist of a remaining small component of very high flow (the arterial phase?) or be an artifact caused by the
obligatory bi-exponential model of calculation. The findings of very small, rapidly perfused compartments and very large, slowly perfused compartments in brain edema is in agreement with the low flow in edematous tissue seen in various experimental studies\textsuperscript{1-3,20,24} in which other methods of measuring and/or calculating rCBF were used.

The results obtained during autoregulation and hyperventilation tests also agree with the results obtained with other methods of calculation. During hypertension, an increase

\begin{figure}
\centering
\includegraphics[width=\textwidth]{hyperventilation_response}
\caption{Hyperventilation response in the same patient as shown in Fig. 4, at a time when he had severe edema. The control flow (left) showed very low rCBF\textsubscript{10} values in the temporal regions. In these areas (shaded areas), the rF\textsubscript{r} values were very high and the rW\textsubscript{r} values very low. During hyperventilation (right), the rF\textsubscript{r} increased and the rW\textsubscript{r} decreased further. In three areas (shaded) adjacent to those just mentioned, the rCBF\textsubscript{10} decreased during hyperventilation to values below 26 ml/100 gm/min, and the flow pattern changed to high rF\textsubscript{r} with low rW\textsubscript{r}. In the remaining areas, the rCBF\textsubscript{10} fell to values of 24 to 30 ml/100 gm/min during hyperventilation, and either the rF\textsubscript{r} or the rW\textsubscript{r} also fell.}
\end{figure}
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in either rFr or in rWf was seen, both indicating an increase of the fast flow compartment (impaired autoregulation), as an increase in rWf may mean that part of the slow compartment had changed to the fast compartment. On the other hand, hyperventilation caused a decrease in rWf indicating that some of the fast compartment had changed to the slow compartment.19,20

In edematous tissue, we found very low rWf values, and the clearance curves had an almost mono-exponential appearance. Several authors9,17,25 have emphasized that Wf is often very low in pathological brain tissue. We presume that the cause of low Wf in patients with severe head injuries is edema, unless the patient has been markedly hyperventilated shortly before the CBF measurement. The high Fr and low Wf from edematous tissue do not reflect flow and weight in the gray matter, but the low Wf does reflect the scantiness of fast flow in the edematous brain tissue.

Various studies have previously shown a decrease in the proportion of the fast clearing tissue (calculated by bicompartmental analysis, and referred to as Wf) in pathological conditions,9,17 and Salmon and Timperman25 have, in addition, demonstrated an increase in both flow and weight of the fast compartments after ventriculoarterial shunting in patients with posttraumatic encephalopathy. Other authors have observed changes in the relative weight of the fast compartment during hyperventilation,19 and during successive injection of 183Xe performed before, during, and after clamping of the internal carotid artery.27

In our series, the relative weight of the fast compartment varied with the nature of the cortical lesions, and it changed during autoregulation and hyperventilation tests. In addition, the weight of the fast compartment changed during the clinical course of the head injury, as the rWf increased during improvement and decreased during deterioration. This is incompatible with an anatomical compartmental division. The weight of the gray and the white matter cannot change between successive injections of 183Xe nor within a few days. We have therefore preferred to use the symbols Fr and Wf instead of the conventional Fg and Wg.

A considerable error in the calculation of CBF is the use of partition coefficients for normal brain tissue in the calculation of flow in pathological brain tissue. Thus O'Brien and Veall14 found different partition coefficients in various brain tumors. The partition coefficients of injured brain tissue are not known, but can be expected to be different from those of normal brain tissue, possibly depending on the type of brain lesion. This error is probably of most importance in the bicompartmental calculation, although it may also influence the rCBF10 and Fr calculation.

Conclusions

Bicompartmental analysis of the clearance curves from patients with head injuries can give important information of the nature and course of the brain lesions, provided the parameters obtained are taken as indicators of fast- and slow-flow compartments, regardless of the anatomical constitution, and provided the results are interpreted properly. The bicompartmental analysis is not ideal for the calculation of blood flow in pathological brain tissue. Without interpretation of the results, the method gives misleading and confusing information. In particular, the function tests are difficult to evaluate, and can only be estimated grossly, as the relative weights of the compartments often change during the tests. The justification of the method is that, provided they are properly interpreted, the results do reflect the pathological processes, and the calculations can be made by means of a computer. Calculation by computer of an initial slope flow index over the first 2 minutes has the same shortcomings as the height/area calculation. It tends to mask fast "third" components. A three-compartmental analysis will probably lead to more uncertain and confusing results, especially because of large parameter errors.7 Most important is the visual inspection of the logarithmically traced clearance curves. This inspection, which is always necessary in order to recognize curve abnormalities and artifacts, can give a quick and focal diagnosis, and thereby be used in the acute clinical situation.

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