ACUTE OCCLUSION OF A MAJOR SUPPLYING ARTERY of the brain results in regional cerebral ischemia, the size and density of which differs considerably from animal to animal. Following transorbital ligation of the middle cerebral artery in cats, blood flow in the center of the supplying territory of this artery varied between 2 and 50 ml/100g/min, and the size of the resulting infarcts between 18 and 62% of the volume of the affected hemisphere. Factors responsible for this variability are differences in blood pressure, intracranial pressure, blood viscosity, vascular resistance of the collaterals, and presumably also the resistance of vessels within the ischemic territory. It is obvious that the main denominator for the degree of ischemia is the local blood perfusion pressure in the territory of the occluded vessel. Measurement of this parameter, in consequence, is of great interest, not only for determination of threshold values for the perfusion of an ischemic region but also for determination of vascular resistance distally to the vascular occlusion.

In the present series of experiments cortical blood perfusion pressure was monitored continuously in the territory of the middle cerebral artery of cat brain by measuring pial arterial blood pressure with a feedback-controlled micropressure recording system. After occlusion of this artery, the changes observed were compared with various physiological, hemodynamic and biochemical parameters in order to obtain a detailed picture of the role of local cortical perfusion pressure on the development of ischemic infarcts. In the first part of this investigation, the general pathophysiological and hemodynamic findings, and in the second part the biochemical observations are described (Paschen et al., in preparation). Some of the results have been published before in abstract form.

Material and Methods

Surgical Procedure

Thirty-three mongrel cats weighing between 2.0 and 3.5 kg were used. The animals were initially anesthetized with 3% halothane, then immobilized with curarine (Pancuronium®), and subsequently ventilated with a gas mixture containing 0.5% halothane, 70% N2O, balance oxygen. Arterial pCO2 was kept between 28 and 30 mm Hg, and arterial pO2 above 100 mm Hg by appropriate adjustment of the animal respirator. Body temperature was kept constant at 37°C with a thermo-controlled heating pad.

The left middle cerebral artery was exposed by the transorbital approach, described by O'Brien and Waltz. The eyeball was deflated and, after cross-cutting the optic nerve, removed. The optic foramen was enlarged with a dental drill under continuous irrigation with cold saline, the dura was split with the sharp tip of a hypodermic needle, and the hook of a small occluder was placed around the middle cerebral artery close to its origin from the internal carotid artery. The surgical procedures were carried out using an operating microscope (Zeiss, Oberkochen, FRG).

Following exposure of the middle cerebral artery, a craniotomy was performed over the parietal region of the ipsilateral hemisphere. A thermocouple was placed on the ectosylvian gyrus for recording of blood flow (see below). The cotton wick of a small calomel electrode was brought into contact with the cortical surface, close to the thermocouple, for recording of EEG and cortical steady potential. A pial artery (diameter
about 100 μ) was punctured on the suprasylvian gyrus under microscopical control with a micropipette for non-occlusive blood pressure measurement, as described below.

All exposed regions of the cortex were covered with saline-soaked cotton balls, and intermittently rinsed with warm saline to prevent drying and cooling of the cortical surface.

After physiological variables had stabilized and control recordings had been carried out, the middle cerebral artery was occluded. The interval between exposure of the artery and occlusion was at least one hour. At the end of the experiment the brain was frozen in situ with liquid nitrogen, as described elsewhere (Paschen et al. in preparation).

Recordings

Blood flow was measured continuously with a heated thermocouple. The instrument was calibrated in gelatine (heat conductance \( \lambda = 12.5 \times 10^{-4} \text{ cal} \times \text{cm}^{-1} \times \text{sec}^{-1} \times \text{°C}^{-1} \)), and changes of cortical blood flow were expressed as changes of heat conductance of cortical surface. At the end of each experiment, cardiac arrest was induced to determine the heat conductance of the unperfused cortex. This measurement was used as a zero flow reference.

CO₂ reactivity was tested by ventilating the animal with 6% CO₂, and autoregulation by increasing systemic arterial pressure. The blood pressure increment was evoked non-pharmacologically by occlusion of the abdominal aorta with an intra-aortal balloon.

Pial artery pressure was measured non-occlusively with a feed-back controlled micropressure recording system. Micropipettes with tip diameter of about 5 μ were filled with 1 M NaCl, and the system was calibrated before and after the experiment by lowering the pipette with a micromanipulator into a cylinder filled with saline.

Steady potential of the cortical surface was measured with small calomel electrodes. The active electrode was placed on the surface of the ectosylvian gyrus, and the indifferent electrode on the occipital bone. EEG was recorded with the same calomel electrode as for D.C. potentials, and the amplified signal was fed into a laboratory computer (PDP12, Digital Equipment, Maynard, MA.) for Fourier frequency analysis. EEG intensity was expressed as the sum of Fourier coefficients covering the range from 0.5 to 20 cps. Amplitude linearization was obtained by calculating the square roots of the coefficients. As a measure of EEG background frequency, an index was calculated by dividing the intensity of the high frequency bands (8 – 20 cps) through that of the low frequency bands (0.5 – 7.5 cps).

All physiological signals were recorded on a polygraph and stored on magnetic tape for offline processing, if necessary.

Results

The pial artery pressure (PAP) was measured non-occlusively in small arteries with a diameter of about 100 μ, located on the surface of the left suprasylvian gyrus (fig. 1, 2). Before occlusion of the middle cerebral artery, mean PAP was 56.2 ± 1.6 mm Hg, and systemic arterial pressure 113.5 ± 2.1 mm Hg (means ± SE, table 1). Immediately after vascular occlusion, PAP fell to 7.8 ± 0.4 mm Hg, i.e., to about 15% of control value. Subsequently, it slightly rose and eventually stabilized at about 15 mm Hg after 2 hours of ischemia. Before vascular occlusion, PAP was pulsatile (fig. 1). After occlusion small respiratory movements but no pulse-synchronous pressure changes were noted.

The decrease of PAP was associated with a decrease of cortical blood flow, measured with a heated thermocouple in the immediate vicinity of the site of pressure recording (fig. 1, 2). Before ischemia cortical heat conductance (\( \lambda \)) averaged 15.1 ± 0.2 × 10⁻⁴ cal × cm⁻¹ × sec⁻¹ × °C⁻¹ (table 1). The mean value of the unperfused cortex, as determined at the end of the experiments, was 10.2 × 10⁻⁴ units. After middle cerebral artery occlusion, heat conductance decreased abruptly to about 10 × 10⁻⁴, but within a few minutes improved and leveled off at a value which was substantially higher than immediately after vascular occlusion (fig. 1). After 15 min average heat conductance was 11.9 ± 0.2 × 10⁻⁴ units, and it remained at this level throughout the observation period of 2 hours (table 1).

The undershoot of blood flow immediately after vascular occlusion was not paralleled by a similar change of pial artery pressure (fig. 1) The improvement of flow during the first minutes of ischemia, in
consequence, can not be explained by a dilatation of the collateral vessels supplying the ischemic territory because this would have resulted in a parallel increase of pial artery pressure, but apparently was the result of a gradual decrease of intracortical vascular resistance.

The simultaneous measurement of cortical heat conductance and pial artery pressure allowed for a semi-quantitative estimation of extra- and intracortical resistance before and after middle cerebral artery occlusion (table 1). Extracortical resistance was defined as the resistance upstream from the pial artery recording and was derived from the blood pressure difference between aorta and pial arteries. Intracortical resistance was defined as the downstream resistance and derived from the pressure difference between the pial arteries and veins. Since the measurements were carried out in an open skull preparation, the latter was neglected. According to this calculation, extracortical resistance after middle cerebral artery occlusion rose from 4.0 to 9.0 mm Hg \( \times \lambda^{-1} \times 10^4 \), and remained at this level throughout the experiment. Intracortical resistance, on the other hand, decreased from 3.6 to 0.7 mm Hg \( \times \lambda^{-1} \times 10^4 \) within 15 min of ischemia, but after 2 hours rose again to 1.2 mm Hg \( \times \lambda^{-1} \times 10^4 \). The gradual increase of intracortical resistance is the reason for the fact that despite the increase of pial arterial pressure in the course of the experiments, blood flow did not improve.

Regulation of blood flow after middle cerebral artery occlusion was severely disturbed, as reflected by the close relationship between spontaneous changes of pial artery pressure and cortical blood flow (fig. 3). The disturbance of autoregulatory capacity was studied in more detail by induced hypertension (fig. 4, table 2). In order to avoid an interference of drug effects with autoregulatory mechanisms, the pressure increment was produced not by infusion of sympathomimetics but by transient occlusion of the abdominal aorta.

Before middle cerebral artery ligation, the change of cortical heat conductance (autoregulatory index) was

| TABLE 1 | Hemodynamic Parameters Before and After Middle Cerebral Artery Occlusion in Cats |
|-------------------------------|-------------------------------|---------------------|---------------------|
|                                | Control (n = 33) | 15 min (n = 32) | 1 hour (n = 25) | 2 hours (n = 25) |
| Pial artery pressure (mm Hg)  | 56.2±1.6          | 7.8±0.4           | 12.9±1.0          | 15.5±0.8          |
| Cortical blood flow* (10^{-4} \times \text{cal} \times \text{cm}^{-1} \times \text{sec}^{-1} \times \text{°C}^{-1}) | 15.1±0.2 | 11.9±0.2 | 12.0±0.2 | 12.0±0.3 |
| Systemic arterial pressure (mm Hg) | 113.5±2.1 | 113.3±2.0 | 112.2±2.3 | 110.6±2.8 |
| Extracortical resistance \((\text{SAP} - \text{PAP}) \times \lambda^{-1} \times 10^6\) | 4.0±0.2 | 9.0±0.2 | 8.6±0.3 | 8.4±0.3 |
| Intracortical resistance \((\text{PAP} \times \lambda^{-1} \times 10^6)\) | 3.6±0.15 | 0.7±0.02 | 1.0±0.06 | 1.2±0.06 |

*Cortical blood flow was expressed as cortical heat conductance (\(\lambda\)). Values are means ± SEM.
Acute middle cerebral artery occlusion in cats. Recording of cortical blood flow (above) and of pial arterial pressure (below).

**FIGURE 4. Autoregulation of blood flow before and after in the territory of the middle cerebral artery.**

less than $4 \times 10^{-6} \text{Hg} \times \lambda^{-1} \times 10^4$, whereas after occlusion, the average increment rose to more than $25 \times 10^{-6} \text{Hg} \times \lambda^{-1} \times 10^4$ (table 2). During the following hour, no improvement of this disturbance occurred.

The increase of flow during induced hypertension contrasted with the behaviour of pial artery pressure (fig. 5). Before ischemia, a pressure increment of 35 mm Hg caused an increase of PAP by about 25 mm Hg, whereas after ischemia the same increment resulted in a rise of pial artery pressure of only 4–7 mm Hg. A considerable portion of the pressure pulse, in consequence, was absorbed by the high resistance of the collateral channels.

This conclusion was corroborated by calculation of the changes of extra- and intracortical vascular resistance (table 2). Before ischemia the autoregulatory adjustment was mainly accomplished by intracortical vessels, the resistance of which increased by $1.63 \text{mm Hg} \times \lambda^{-1} \times 10^4$. The resistance increment of extracortical vessels was much less and amounted to $0.64 \text{mm Hg} \times \lambda^{-1} \times 10^4$. Shortly after middle cerebral artery occlusion, the same pressure pulse caused an increase of intracortical resistance by less than $0.3 \text{mm Hg} \times \lambda^{-1} \times 10^4$, whereas the increase of extracortical resistance rose to almost $2 \text{mm Hg} \times \lambda^{-1} \times 10^4$. This demonstrates that following middle cerebral artery occlusion, the collateral vessels supplying the ischemic territory autoregulate and therefore reduce the blood supply to this region.

Two hours after the beginning of ischemia, autoregulation was partly restored. This response is presumably "false" autoregulation due to developing intracortical edema because it correlated with the spontaneous rise of intracortical vascular resistance (table 1).

CO$_2$-reactivity of the cortical vasculature was studied by ventilating the animal with 6% CO$_2$ (fig. 5, table 3). Before ischemia, hypercapnia induced a decrease of PAP by about 18 mm Hg; after ischemia, PAP did not change during CO$_2$ ventilation. The CO$_2$ index of blood flow before ischemia amounted to $56 \lambda \times 10^{-6} \text{mm Hg}^{-1} \text{apCO}_2$ (table 3). The increase of flow was entirely due to a reduction of intracortical resistance which decreased by $1.43 \text{mm Hg} \lambda^{-1} \times 10^4$. Extracortical resistance, in contrast, distinctly increased by $1.15 \text{mm Hg} \lambda^{-1} \times 10^4$, i.e. a value which is far more than could be expected from the associated rise of arterial pressure during CO$_2$ ventilation. After middle cerebral artery occlusion CO$_2$-reactivity was completely abolished or even reversed, as indicated by the slight increase in intracortical resistance. Resistance of extra-cortical vasculature did not change in contrast to the distinct rise before ischemia. The collaterals, in consequence, seem to dilate under CO$_2$ and thereby compensate the resistance increment of the proximal segment of the vascular bed.

Electrocortical activity was recorded before and after middle cerebral artery occlusion from the same cortical region in which PAP was monitored. Immediately after vascular occlusion, EEG intensity declined to about 50% of the pre-ischemic value and in most animals remained at this level throughout the experiment (fig. 2). The changes of EEG background frequency were less dramatic. The EEG frequency index...

**TABLE 2. Autoregulation of Cortical Blood Flow Before and After Middle Cerebral Artery Occlusion in Cats**

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 10)</th>
<th>15 min (n = 10)</th>
<th>1 hour (n = 10)</th>
<th>2 hours (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic arterial pressure increase (mm Hg)</td>
<td>35.5±3.2</td>
<td>32.5±3.2</td>
<td>35.0±4.0</td>
<td>33.5±4.5</td>
</tr>
<tr>
<td>Pial artery pressure increase (mm Hg)</td>
<td>24.9±1.5</td>
<td>4.3±0.5</td>
<td>6.8±0.9</td>
<td>5.3±0.8</td>
</tr>
<tr>
<td>Cortical blood flow increase* (λ x 10^{-4})</td>
<td>0.12±0.04</td>
<td>0.85±0.13</td>
<td>0.86±0.13</td>
<td>0.45±0.10</td>
</tr>
<tr>
<td>Autoregulatory index (λ x 10^{-6} x mm Hg^{-1})</td>
<td>3.8±1.3</td>
<td>27.4±3.6</td>
<td>27.4±5.0</td>
<td>13.3±2.5</td>
</tr>
<tr>
<td>Extracortical resistance increase ((SAP - PAP) x λ^{-1} x 10^4)</td>
<td>0.64±0.21</td>
<td>1.60±0.22</td>
<td>1.47±0.32</td>
<td>2.02±0.30</td>
</tr>
<tr>
<td>Intracortical resistance increase (PAP x λ^{-1} x 10^4)</td>
<td>1.63±0.10</td>
<td>0.28±0.04</td>
<td>0.47±0.09</td>
<td>0.41±0.06</td>
</tr>
</tbody>
</table>

*Cortical blood flow is expressed as cortical heat conductance (λ). Values are means ± SEM.
Blood flow: before ischemia during ischemia

Pial art. pressure: before ischemia during ischemia

**FIGURE 5.** $CO_2$ reactivity of blood flow before and after acute middle cerebral artery occlusion. Recording of cortical blood flow (above) and of pial arterial pressure (below) in the territory of the middle cerebral artery.

— which is the ratio of fast to slow frequency intensity — decreased by only 20%. The predominance of EEG amplitude versus frequency changes was also reflected by the relationship with pial artery pressure (fig. 3). A significant correlation existed between PAP and EEG intensity, but not with EEG frequency index. Acute reduction of cortical perfusion pressure, in consequence, affects mainly the amplitude but to a much lesser degree the frequency content of electrocortical activity.

The cortical steady potential shifted after middle cerebral artery occlusion towards negativity (fig. 1, 2). The shift began after about 30 sec, initially at a slow and later at an accelerating rate until, after 2–3 min, steady potential sharply declined to a level somewhere between $-5$ and $-13 \text{ mV}$. The average DC potential after 15 min was $9.1 \pm 0.7 \text{ mV}$ below the pre-ischemic level. In the individual experiment the level of the steady potential shift was a function of cortical perfusion pressure (fig. 3). In analogy to the changes of EEG intensity, decreasing PAP caused an increasing shift of DC potential. In some animals in which PAP spontaneously rose in the course of the experiment, the DC potential also improved. However, this was not a consistent finding, and the average DC potential shift remained at the same level throughout the experiment despite the slight increase of PAP.

**Discussion**

Non-occlusive pial artery pressure measurements have been carried out by several authors in normal animals for determination of the localization of cerebro-vascular resistance. The results obtained are very similar to our pre-ischemic recordings: the pressure in pial arteries with a diameter of about 100 $\mu$m was 50–70% of that in the aorta. The pressure decrease across pial arteries is relatively low: 5–15% according to Fox and Stromberg, and about 10% according to Dieckhoff and Kanzow. Vascular resistance, in consequence, is built up mainly by the large supplying arteries and the intracortical arteries, and to a much lesser degree by the pial arteries. The relatively small pressure change across the pial arteries is a methodological advantage because irritative changes of pial artery diameter by the micropipette or differences in the diameter of the sampled segments are associated only with minor changes of pressure. Pial artery pressure recording, in consequence, is a simple and reliable approach to assess local cortical perfusion pressure, and to evaluate the respective role of extra- and intracranial vasculature for regulation of cerebral blood flow under physiological and pathophysiological conditions.

To our knowledge, none of the previous non-occlusive recordings of pial artery pressure was combined with quantitative or semi-quantitative measurements of blood flow. It, therefore, was only possible to assess the ratio of extra- to intracerebral vascular resistance, but not absolute changes of these parameters. In the present investigation, cortical heat conductance was monitored continuously for assessing cortical blood flow in the immediate vicinity of the pressure recording. Although only a semi-quantitative method, changes of heat conductance faithfully reflect similar

### Table 3 $CO_2$ Reactivity of Cortical Blood Flow Before and After Middle Cerebral Artery Occlusion in Cats

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 10)</th>
<th>15 min (n = 10)</th>
<th>1 hour (n = 10)</th>
<th>2 hours (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial pCO$_2$ increase (Torr)</td>
<td>26.6±1.3</td>
<td>28.7±0.8</td>
<td>29.4±1.1</td>
<td>28.9±1.1</td>
</tr>
<tr>
<td>Pial artery pressure change (mm Hg)</td>
<td>$-17.6±1.5$</td>
<td>1.4±0.4</td>
<td>2.0±0.9</td>
<td>1.5±0.5</td>
</tr>
<tr>
<td>Cortical blood flow increase* ($k \times 10^{-4}$)</td>
<td>1.48±0.018</td>
<td>0.06±0.14</td>
<td>0.16±0.19</td>
<td>0.24±0.14</td>
</tr>
<tr>
<td>Systemic arterial pressure increase (mm Hg)</td>
<td>7.0±1.1</td>
<td>4.0±1.0</td>
<td>4.3±1.9</td>
<td>7.0±1.1</td>
</tr>
<tr>
<td>CO$_2$ index ($\lambda \times 10^{-6} \times \text{mm Hg}^{-1}$)</td>
<td>56.3±4.7</td>
<td>2.0±5.0</td>
<td>5.7±6.8</td>
<td>12.9±3.8</td>
</tr>
<tr>
<td>Extracortical resistance change ((SAP - PAP) $\times \lambda^{-1} \times 10^9$)</td>
<td>1.15±0.13</td>
<td>0.20±0.11</td>
<td>0.07±0.20</td>
<td>0.29±0.13</td>
</tr>
<tr>
<td>Intracortical resistance change ($PAP \times \lambda^{-1} \times 10^9$)</td>
<td>$-1.43±0.10$</td>
<td>0.12±0.04</td>
<td>0.16±0.06</td>
<td>0.10±0.03</td>
</tr>
</tbody>
</table>

*Cortical blood flow was expressed as cortical heat conductance ($\lambda$). Values are means ± SEM.
changes of blood flow, and therefore can be used for determining directional changes of extra- and intracortical resistance.

Such a calculation, however, assumes that blood flow is conducted across resistances coupled in series. This assumption is questionable in view of the anatomical configuration of the intracortical vascular bed, and is undoubtedly wrong as far as the extracortical vasculature is concerned. After middle cerebral artery occlusion blood supply to the ischemic territory is mainly by Heubner’s pial anastomoses which form a multiple-branched network on the surface of the cerebral cortex. Blood flow, in consequence, is conducted through a system of parallel resistances, the respective participation of which in total vascular resistance is impossible to evaluate. By simplification, however, the resistance network upstream from the pial artery recording site may be lumped into one global resistance, the changes of which can, in fact, be described quantitatively. The results obtained, therefore, do not refer to a given branch of the vascular bed but to the total vascular system up- or downstream from the pial artery pressure head.

Using this approach, the participation of the extra- and intracortical vasculature for flow regulation was evaluated before and after middle cerebral artery occlusion. Already in the normal state, a striking difference of the responsiveness of extra- and intracortical vessels was noted in respect to changes of blood pressure and arterial pCO₂. During induced hypertension, approximately 30% of total resistance changes were built up by extracortical arteries, whereas flow increase during hypercapnia was entirely due to dilatation of intracortical vessels. Surprisingly, resistance of extracortical vessels paradoxically increased during ventilation with carbon dioxide, a phenomenon which has not been described before. The difference in the anatomical localization of resistance regulation during autoregulation and CO₂-reactivity is in line with previous observations and is one of the many arguments against a unified hypothesis for hemodynamic and metabolic flow regulation.

Following middle cerebral artery occlusion, pial artery pressure fell to about 20% of the pre-ischemic value. This value is of the same order of magnitude as in previous investigations, and corresponds to the pressure range of 10–16 mm Hg predicted in a computer model of simulated middle cerebral artery occlusion. Cortical heat conductance after middle cerebral artery occlusion decreased from 15.1 to 11.9 × 10⁻⁴ cal × cm⁻¹ × sec⁻¹ × °C⁻¹. Heat conductance of the non-perfused cortex after cardiac arrest is 10.2; blood flow, in consequence, fell to about 30%, which is also in line with previous quantitative measurements.

Symon and coworkers reported in the sixties an experimental investigation of pial artery pressure following middle cerebral artery occlusion in dogs and monkeys. This study is not directly comparable with the present one because pial artery pressure was measured with small catheters which occluded the vessel lumen, a methodological difference which presumably accounts for the fact that prior to ischemia pial blood pressure amounted up to 95% of femoral artery pressure. During ischemia, an interesting difference was noted between the two species: in monkeys pial artery pressure remained stable at a level of about 25 mm Hg, but a considerable increase to almost 40 mm Hg was observed in dogs, indicating a gradual improvement of collateral blood supply in the latter species. Our results in cats are closer to the monkey model; we observed an improvement by only about 7 mm Hg which suggests that in cats delayed collateralization of the ischemic territory is of minor importance.

Pial artery pressure, over a wide range, correlated with blood flow as well as with EEG amplitude and the cortical steady potential. There was no threshold relationship between these parameters; it appeared, however, that critical ischemia as previously defined occurs at a local perfusion pressure between 5 and 10 mm Hg because at this pressure electrophysiological disturbances become most pronounced.

As expected, intracortical vascular resistance after middle cerebral artery occlusion decreased, and cortical vessels did not respond to either changes of systemic arterial pressure or arterial pCO₂. The slight improvement of autoregulatory index a few hours after onset of ischemia is presumably false autoregulation as a consequence of increased regional tissue perfusion pressure during the development of ischemic brain edema. These findings are in agreement with the long known phenomenon of vasoparalysis and total abolishment of flow regulation under ischemic conditions.

The new and probably most important aspect of the present investigation is the reactivity of extracortical vasculature after middle cerebral artery occlusion. It is obvious that the increment of extracortical resistance after vascular occlusion reflects the resistance of the collaterals supplying the ischemic territory, in particular Heubner’s pial anastomoses. Extracortical resistance changes during induced hypertension or hypercapnia, therefore, can be interpreted mainly as a response of these vessels. The results obtained suggest that the collaterals react to such changes in a similar way as normal brain vessels. This has been well-documented for induced hypertension which caused a considerable increase in extracortical vascular resistance. During CO₂ inhalation extracortical resistance did not change. However, this is probably not due to a loss of CO₂ reactivity of the collateral vessels, but the net effect of proximal (large vessels) vasoconstriction and distal (collateral vessels) vasodilation, as suggested by the relative decrease of resistance in comparison to the pre-ischemic situation.

These findings have several interesting therapeutic implications. The fact that collateral vessels are not rigid in a hemodynamic sense, suggests that they may be accessible to pharmacologically induced vasodilation. Such a vasodilation would result in a considerable improvement of flow, as demonstrated by computer simulations of middle cerebral artery occlusion. Even prevention of autoregulatory vasoconstriction of the collaterals would be of importance because the present
findings demonstrate that a slight improvement of local pial artery pressure above the critical value of 5–10 mm Hg considerably improves blood flow and electrocortical function. A maximum effect can be expected by combining pharmacologically induced vasodilation and mild hypertension. Pial artery pressure recording would be most useful to optimize this approach.

Another conclusion concerns the possible use of hypercapnia for improving blood flow. In previous studies considerable disagreement has been expressed about the presence or absence of steal phenomena and, in consequence, about the potential usefulness of hypercapnia for the treatment of stroke. If the interpretation of our results is correct, the failure of improving blood flow by hypercapnia is due to the fact that vasodilation of collaterals is counteracted by the simultaneous vasoconstriction of the peripheral segments of the extracranial vascular bed. The combination of CO₂ inhalation with vasodilating agents, therefore, may be of benefit. Also, this approach could be tested under continuous monitoring of pial artery pressure.

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