Distributions of Local Oxygen Saturation and Its Response to Changes of Mean Arterial Blood Pressure in the Cerebral Cortex Adjacent to Arteriovenous Malformations

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Background and Purpose—To test the hypothesis that neither “steal” as cortical ischemia caused by reduced perfusion pressure nor “breakthrough” on the grounds of loss of pressure autoregulation exist in brain tissue surrounding arteriovenous malformations (AVMs), we established patterns of cortical oxygen saturation (SO2) adjacent to AVMs and its behavior after alterations of mean arterial blood pressure.

Methods—With a microspectrophotometer, SO2 was scanned in the cortex around AVMs of 44 patients before and after resection and in that of a non-AVM group (n=42) before transsylvian dissection. Autoregulation was evaluated by linear regression analysis after elevation of mean arterial blood pressure (5 μg/min IV noradrenaline). SO2 values were calculated as medians, percentage of critical values (<25% SO2), and coefficients of variance (approximate heterogeneity of SO2 distributions). All values are given as mean±SD.

Results—Forty patients with AVM had an uneventful postoperative course (group A). Four hyperemic complications (“breakthrough”) occurred (group B). Autoregulation was tested intact in all groups at all times. Preoperative SO2 distributions in groups A and C (non-AVMs) were identical. In group B, significantly (P<0.05) lower medians (group A, 52.9±16.3%; group B, 44.2±17.1%; group C, 51.9±11.5% SO2), more critical values (group A, 6.5±5.1%; group B, 14.7±11.1%; group C, 7.1±4.9%), and heterogeneous SO2 distributions (group A, 20.2±12.7%; group B, 27.9±12.4%; group C, 26.8±10.9%) were seen. Increase of median values was significantly higher in group B (76.3±10.4% SO2) than in group A (65.9±13.4% SO2) after resection.

Conclusions—Severely hypoxic areas are uncommon in the cortex adjacent to AVMs and occur predominantly in patients prone to hyperemic complications. Reduced perfusion pressure is compensated in most cases, and moderate hyperemia prevails after excision. Reperfusion into unprotected capillaries of severely hypoxic cortical areas results in “breakthrough,” for which vasoparalysis appears not to be the underlying mechanism. (Stroke. 1999;30:2623-2630.)

Key Words: autoregulation ■ cerebral arteriovenous malformations ■ cerebrovascular circulation ■ oxygen

It has long been described in a qualitative manner that cerebral arteriovenous malformations (AVMs) induce alterations of cerebral blood flow in the surrounding brain tissue and that these alterations are closely related to pathophysiological events occurring after the exclusion of AVMs from the cerebral circulation,1 some of which still have disastrous consequences for a considerable percentage of patients.2 It seemed plausible that AVMs generate an ischemic environment in the surrounding cortex and that their exclusion causes a hyperemic response.3 Certain labels were attributed to these situations such as preoperative “steal” and postoperative “breakthrough” in the case of edema formation or hemorrhage.1,4

A theory was formulated in 1978 derived from clinical observations and animal experiments (Normal Perfusion Pressure Breakthrough Theory, NPPB).4 It was postulated that AVMs cause a reduction of cerebral perfusion pressure (CPP), which induces a maximum reduction of cerebrovascular resistance (CVR) in the surrounding brain tissue to the point where ischemia occurs and cerebral pressure autoregulation is lost. Closure of the arteriovenous shunt system then normalizes perfusion pressure, but autoregulatory capacity is not restored in certain cases, which is the underlying mechanism for a “breakthrough.”

The problem for nearly the next 2 decades was that none of these phenomena could be pinpointed without reasonable doubt in patients. Neither “steal” nor “hyperemia” could be reliably quantified in most studies. Ambiguous results obtained after testing of CO2 reactivity were subject to controversial interpretations, and assumptions were made on pres-
sure autoregulation, which was never tested itself. Some misconceptions arose from the neglect of the heterogeneity of cerebral blood flow under physiological conditions and/or the use of methods with insufficient resolution. Furthermore, results obtained by measurements of “shunt flow” (within the AVM system) were used to deduce assumptions on “perfusion flow” (within the surrounding tissue).

In some recent studies, however, solid evidence for several aspects of AVM pathophysiology was presented. It was demonstrated that the AVM-induced reduction of CPP did not cause a maximum reduction of CVR in the adjacent cortex of patients with AVM because further arteriolar relaxation was possible in every case. Preoperative CBF levels in patients with AVM were seemingly not lower than in control patients. Pressure autoregulation—tested for the first time—appeared to be intact before and after resection of AVMs. These results called into question the classic concepts of “steal” in the sense of cortical ischemia as a consequence of reduced CPP and “breakthrough” on the grounds of loss of pressure autoregulation. It was concluded that if these phenomena occur, the pathophysiological mechanism responsible is obviously not at the arteriolar level and probably multifactorial. Doubts regarding their results and conclusions were expressed by the same authors because of the insufficient temporal and spatial resolution of the method used, which did not allow insights into the microenvironment of the surrounding cortex. Their findings with regard to intact pressure autoregulation so far have not been corroborated in general and in the event of a “breakthrough” in particular.

We therefore initiated a systematic intraoperative study on patients with AVM by using a technique that quantifies cortical capillary oxygen saturation (SO2) with high temporal and spatial resolution. Our aims were primarily to establish patterns of oxygen supply in cortical microcirculatory units adjacent to AVMs before and after their resection and behavior of SO2 after induced alterations of systemic blood pressure. Because cerebral oxygen metabolism was assumed to be constant during the experiments, changes in SO2 were interpreted to reflect primarily changes of regional CBF.

Subjects and Methods
This study was approved by the local ethics review committee. Written consent was obtained from all patients for the experiments at least 24 hours before the operation.

Measurements of Intracapillary Oxygen Saturation
Values of intracapillary SO2 were measured with the Erlangen Microlightguide Spectrophotometer (EMPHO II, Bodenseewerk Gerätetechnik GmbH, BGT), which was introduced in 1989. It was designed for fast, diffuse remission spectrophotometry by flexible microlight guides in small tissue volumes of moving organs in situ. Light in the visible domain illuminates tissue by means of the illuminating fiber, and backscattered light is transmitted by 6 detecting fibers (Ø 70 μm)—arranged in a hexagonal pattern around the illuminating fiber—to a rotating bandpass interference filter disk. This serves as a monochromating unit in the spectral range of 502 to 628 nm in 2-nm steps. Spectra of 64 wavelengths per rotation are thus transmitted to a photomultiplier, an AD-converter, and finally to a computer, in which 1 SO2 value per spectrum is calculated by algorithms described elsewhere. The obtained SO2 values reliably indicate oxygen transport to tissue and indirectly nutritive capillary flow (see Discussion). The high temporal (100 spectra/s) and spatial (75×250 μm) resolution permits an easy scanning procedure of superficial cortical capillaries by moving the light guide above the brain surface.

Study Groups and Protocol
Forty-four patients (19 female patients, 25 male patients, mean age 32 years, range 5 to 66 years) harboring cerebral AVMs of Spetzler/Martin grades I (n=4), II (n=19), III (n=15), and IV (n=6) were included in the study. All underwent elective microsurgery for complete resection of the malformations. SO2 distributions were measured by scanning an average of 5 small (≈5 mm2) areas (≈300 to 500 SO2 values per area and measurement) of the exposed cortex surrounding the AVM before and after the resection at distances 2 to 4 cm from the nidus (approximate resection margin). All areas were numbered and photographed documented under the highest magnification of the operating microscope for exact postoperative relocation. Areas in which surgical trauma was suspected by microscopic inspection or otherwise (eg, close to resection margin) were excluded from postoperative measurements.

Preoperative and postoperative behavior of cortical SO2 after alterations of mean arterial blood pressure (MABP) was established by simultaneous, continuous monitoring of MABP (radial artery) and SO2 in identical cortical areas before and after surgery. MABP was elevated 40% above baseline (≈30 mm Hg) by continuous intravenous infusion of 5 μg/min noradrenaline. Under the assumption that alterations of SO2 depend predominantly on alterations of flow, the observed behavior was considered a measure of cerebral pressure autoregulation. Nineteen patients in the AVM group gave their consent to undergo the test.

Forty-two patients (24 female patients, 18 male patients, mean age 36 years, range 14 to 72 years) underwent transsylvian microsurgery for deep-seated nonvascular lesions. Deep-seated lesions were selected to obtain baseline values of SO2 distributions in normal frontal and temporal cortex uncompromised by any space-occupying process. This group was matched to the AVM group with respect to ASA classification. SO2 distributions (n=42) and pressure autoregulation (n=20) were established with the protocol described above before the start of the transsylvian dissection.

For all operations, total intravenous anesthesia was induced with 1.5 mg/kg propofol (maintained with 5 to 10 mg/kg per hour), 15 μg/kg alfentanil (maintained with 0.1 to 0.2 mg/kg per hour), and 0.1 mg/kg vecuronium (maintained with 30 to 60 μg/kg per hour) under inhalation of 40% O2 and 60% N2. MABP and heart rate were monitored continuously with a radial artery line. Arterial blood samples (PaO2, PaCO2, pH) and venous blood samples (hematocrit) were taken at times of SO2 measurements.

Data Analysis
SO2 values were pooled according to groups and times of measurements and displayed as frequency histograms. They were calculated as medians [% SO2] and ratios of critical values [%] defined as percentage of SO2 values <25% SO2, which approximately corresponds to a cerebral venous PO2 of 12 mm Hg. Coefficients of variance [%] (SD/mean×100%) were calculated to approximate heterogeneity of SO2 distributions depending (under conditions of constant arterial oxygen supply and consumption) primarily on erythrocytic capillary flow. Coefficients of variance (CV) were thus interpreted as a the numerical expression of heterogeneity of nutritive capillary flow velocities as described elsewhere.

ANOVA, Wilcoxon (dependent, nonparametric variables), and Kolmogorov-Smirnov (independent, cumulative variables) tests were used for statistical analysis, with a level of significance set at P<0.05. All values are given as mean±SD.

Adopting an algorithm described previously (ie, Reference 25), pressure autoregulation was evaluated by linear regression analysis of SO2 on MABP, with MABP used as the independent variable. Time intervals with continuous rise of MABP from baseline to peak level were used for calculations. Two criteria were applied to define intact autoregulation (ie, absence of vasoparalysis): (1) the calculated
TABLE 1. Data From Arterial Blood Gas Analyses, Venous Hematocrits, and MABP Obtained at Times of Measurements of Cortical Capillary So2

<table>
<thead>
<tr>
<th>Group</th>
<th>A (Pre)</th>
<th>A (Post)</th>
<th>B (Pre)</th>
<th>B (Post)</th>
<th>C (Non-AVMs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n</td>
<td>40</td>
<td>40</td>
<td>4</td>
<td>4</td>
<td>42</td>
</tr>
<tr>
<td>Hct, vol%</td>
<td>34±5</td>
<td>33±5</td>
<td>35±4</td>
<td>34±4</td>
<td>35±4</td>
</tr>
<tr>
<td>PaCO2, mm Hg</td>
<td>29.7±2.6</td>
<td>29.9±2.3</td>
<td>30.1±2.8</td>
<td>29.3±2.1</td>
<td>30.0±2.6</td>
</tr>
<tr>
<td>pH</td>
<td>7.47±0.04</td>
<td>7.47±0.03</td>
<td>7.47±0.04</td>
<td>7.48±0.02</td>
<td>7.48±0.05</td>
</tr>
<tr>
<td>PaO2, mm Hg</td>
<td>216±29</td>
<td>215±31</td>
<td>218±32</td>
<td>217±28</td>
<td>214±31</td>
</tr>
<tr>
<td>MABP, mm Hg</td>
<td>76±13*</td>
<td>82±12</td>
<td>79±11</td>
<td>81±9</td>
<td>80±10</td>
</tr>
</tbody>
</table>

Group A indicates patients with AVM without postoperative hyperemic complications; group B, patients with AVM with postoperative hyperemic complications; and group C, patients without AVM.

Measurements were taken before (pre) and after (post) resection of malformations in patients with AVM and before transf Sylvian dissection in patients without AVM. Values are given as mean±SD.

Results

Patients with AVM were subdivided according to their postoperative clinical course into group A (n=40) if uneventful or group B (n=4) if breakthrough (in the following referred to as hyperemic complication) occurred. Hyperemic complications were defined as clinical deteriorations caused by the occurrence of otherwise unexplainable postoperative edema and/or hemorrhage on computed tomography scans. Incomplete AVM resection or other causes were ruled out on postoperative angiograms. Definition of hyperemic complications was performed according to clinical and radiological criteria by the senior author (J.S.) and neuroradiologists, both blinded to So2 data. Patients without AVM constituted group C.

Physiological variables showed no significant differences among groups and times of measurements for blood gases and hematocrit. Only MABP values in group A before resection were significantly lower (Table 1).

Comparison of pooled data as histograms and calculated parameters of cortical capillary So2 showed no significant difference in median values and ratio of critical values between patients with AVM without postoperative hyperemic complications (group A: median 52.9±16.3% So2, ratio of critical values 6.5±16.3%) and control subjects (group C: median 51.9±11.5% So2, ratio of critical values 7.1±9.9%). Only an insignificant increase of very low So2 values in group A was noticed. Significantly less heterogeneous So2 distribution in group A (CV 20.2±12.7%) than in group C (CV 26.8±10.9%) was observed. Median So2 values (44.2±17.1% So2) in patients with AVM with postoperative hyperemic complications (group B) were significantly lower and the ratio of critical values (14.7±30.1%) significantly higher than in groups A and C. So2 distributions in group B (CV 27.9±22.4%) were more heterogeneous than in group A (Table 2 and Figure 1).

Detailed analysis of So2 distribution in group B revealed median values as low as 20% So2, a ratio of critical values as high as 60%, and CVs up to 70% in individual areas.

TABLE 2. Mean Values of Calculated Parameters for Pooled Capillary So2 Distributions in Cortex Adjacent to AVMs Before and After Resection and in Patients Without AVM Before Trans Sylvian Dissection

<table>
<thead>
<tr>
<th>Group</th>
<th>A (Pre)</th>
<th>A (Post)</th>
<th>B (Pre)</th>
<th>B (Post)</th>
<th>C (Non-AVMs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n</td>
<td>40</td>
<td>40</td>
<td>4</td>
<td>4</td>
<td>42</td>
</tr>
<tr>
<td>Total So2 values, n</td>
<td>71780</td>
<td>65474</td>
<td>5934</td>
<td>5069</td>
<td>51340</td>
</tr>
<tr>
<td>Median, % So2</td>
<td>52.9±16.3</td>
<td>65.9±13.4*</td>
<td>44.2±17.1†</td>
<td>76.3±10.4‡</td>
<td>51.9±11.5</td>
</tr>
<tr>
<td>Ratio of critical values, %</td>
<td>6.5±17.1</td>
<td>0.8±4.4*</td>
<td>14.7±30.1†</td>
<td>0.7±2.7§</td>
<td>7.1±9.9</td>
</tr>
<tr>
<td>Coefficient of variance, %</td>
<td>20.2±12.7‖</td>
<td>11.5±6.6*</td>
<td>27.9±22.4</td>
<td>11.1±8.3§</td>
<td>26.8±10.9</td>
</tr>
</tbody>
</table>

Group A indicates patients with AVM without postoperative hyperemic complications; group B, patients with AVM with postoperative hyperemic complications; and group C, patients without AVM.

Measurements were taken before (pre) and after (post) resection of malformations in patients with AVM and before trans Sylvian dissection in patients without AVM.

Different from (P<0.05), †comparison with A (pre) and C; ‡comparison with A (pre) and C; ‖comparison with B (pre) and A (post); §comparison with B (pre) and C. Values are given as mean±SD.
6.3% SO₂) was significantly higher than in patients with AVM with hyperemic complications (group B) higher SO₂ values) in the frequency histograms of groups A and B as opposed to groups A and C. Gaussian SO₂ distributions were predominant in individual areas of the latter groups, and calculated SO₂ parameters were preferentially similar to the pooled data.

A significant shift to the right of the distributions (toward higher SO₂ values) in the frequency histograms of groups A and B was observed after the resection of the AVMs. Pooled group data correspondingly revealed a significant decrease of the ratio of critical values (group A 0.8±4.4%, group B 0.7±2.7%) and of CV (group A 11.5±6.6%, group B 11.1±8.3%). However, the increase of median SO₂ in patients with AVM with hyperemic complications (group B 76.3±10.4% SO₂) was significantly higher than in patients with an uneventful postoperative course (group A 65.9±13.4% SO₂) (Table 2 and Figure 2).

Detailed analysis of the SO₂ distributions in group B after the resection of the AVMs showed the highest SO₂ levels, preferentially within those areas with the lowest preoperative oxygen supply.

During the tests of pressure autoregulation in the control group (group C), 18 of 20 linear regressions reached statistical significance (P<0.05). Mean elevation of MABP above baseline was +39±13%, with an average velocity of induced blood pressure change of +0.14±0.07 mm Hg/s (+37±12%, respectively, +0.13±0.08 mm Hg/s after excision). Mean slope of all significant regression lines was +0.02±0.20% SO₂/mm Hg (range +0.32% to 0.41% SO₂/mm Hg) before surgery and +0.02±0.17% SO₂/mm Hg (range +0.28 to 0.37% SO₂/mm Hg) after surgery. None of the slopes exceeded the critical slope of +0.4% SO₂/mm Hg. Thus autoregulation was considered intact in all patients tested in the AVM group before and after the resection of the malformations regardless of the occurrence of hyperemic complications (Table 3 and Figure 3).

Discussion

Methodology

The potential drawback of the microspectrophotometric technique (ie, the EMPHO II) applied in this study, has been discussed previously.26 It lies in the lack of an exact validation for brain tissue, through which assumptions in the algorithm might eventually be violated. This is, however, only of interest with respect to exact assessment of truly absolute SO₂ values in the brain. The absolute data gathered.
TABLE 3. Data for Behavior of SO2 After Induced Elevation of MABP (Autoregulation Tests) in Patients With and Those Without AVM Before and After Resection of Malformation

<table>
<thead>
<tr>
<th></th>
<th>AVMs (Pre)</th>
<th>AVMs (Post)</th>
<th>Non-AVMs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients tested, n</td>
<td>19</td>
<td>18</td>
<td>20</td>
</tr>
<tr>
<td>Intact autoregulations, n</td>
<td>19</td>
<td>18</td>
<td>20</td>
</tr>
<tr>
<td>Significant regressions, n</td>
<td>18</td>
<td>16</td>
<td>18</td>
</tr>
<tr>
<td>MABP elevation from baseline, %</td>
<td>+39±13</td>
<td>+37±12</td>
<td>+42±16</td>
</tr>
<tr>
<td>Velocity of MABP change, mm Hg/s</td>
<td>+0.14±0.07</td>
<td>+0.13±0.08</td>
<td>+0.20±0.09</td>
</tr>
<tr>
<td>Slope of regression lines, % SO2/mm Hg</td>
<td>+0.02±0.20</td>
<td>+0.02±0.17</td>
<td>+0.02±0.18</td>
</tr>
<tr>
<td>Range</td>
<td>+0.32 to −0.41</td>
<td>+0.28 to −0.37</td>
<td>+0.26 to −0.40</td>
</tr>
</tbody>
</table>

Behavior of SO2 was considered indicative for intact autoregulation if (a) linear regression analysis was not significant (P<0.05) or (b) the slope of the regression line did not exceed the critical value of +0.4% SO2/mm Hg. All values are given as mean±SD.

by the EMPHO II are identical to those obtained by other systems used for intravital microreflectometry under comparable conditions. This shows that even the error for absolute readings of cortical SO2 is probably minor.

Moreover, it has now been demonstrated reliably that the obtained SO2 values reflect tissue oxygenation very accurately because simultaneous recordings of SO2 with the EMPHO II and tissue oxygen partial pressure (PtO2) with multiwire surface electrodes have shown an excellent correlation over a wide range (20% to 80% SO2) of arterial oxygenation levels. Under constant arterial oxygen supply and oxygen consumption, the SO2 readings obtained by this technique reflect changes of nutritive capillary flow with a very high sensitivity, as evidenced by simultaneous measurements of SO2 (EMPHO II) and CBF (laser Doppler flowmetry). Furthermore, it could be demonstrated under conditions of hypoxic or anemic hypoxia as well as ischemia that capillary saturation levels may fall below venous SO2, a situation similar to the one observed in group B. Although exact validation of very low SO2 values does not exist, we consider it therefore a true assumption that such a configuration of SO2 distributions indicates severe tissue hypoxia or ischemia.

For these reasons, we thought this technique to be ideal for the questions to be answered in this study, that is, the supply situation in microcirculatory units of the cortex surrounding cerebral AVMs. Besides its sufficient spatial resolution, the apparatus permits an easy and fast scanning procedure in a “no-touch” technique because of its high temporal resolution.

Another methodological problem to be discussed is the evaluation of pressure autoregulation. We consider it a valid assumption that the behavior of SO2 after alterations of MABP under constant conditions is almost exclusively a function of local CBF. This has also been shown in recent studies, which measured cerebrovascular reactivity reliably by means of near-infrared spectroscopy (eg, see Reference 27), although the relation of SO2 and CBF is theoretically nonlinear. This is consistent with the trend to use estimates such as CBF velocity for dynamic testing of cerebral autoregulation.

In our opinion, the problem lies within the algorithm and even more the definition of pressure autoregulation. Although we performed a dynamic measurement as opposed to static testing, which has also been applied in the aforementioned AVM studies, linear regression analysis allows only for definition of intact versus lost autoregulation by an arbitrary cutoff line. The problem that no “gold standard for quantification of autoregulation” exists has been acknowledged in all previous publications. Very recently developed, more complex algorithms will probably enhance sensitivity and allow for a better quantification and grading of cerebral pressure autoregulation. Yet even with the application of these algorithms, the decision that calculated value indicates an disturbance remains arbitrary. We think that our method enabled us to achieve our primary goal, that is, to rule out major disturbances of autoregulation such as complete vasoparalysis, postulated to be the underlying mechanism of “breakthrough.” This assumption is corroborated by the fact that the patterns of SO2 behavior after induced alterations of MABP within the brain tissue surrounding AVMs are strikingly similar to those measured in normal cortex.

Preoperative Steal Syndrome
In contrast to previous studies, we have shown that the proven reduction of CPP in brain-nutritiving branches of arterial feeding arteries does not cause lowered tissue oxygenation in the vast majority of patients with AVMs. This is in accordance with recent publications giving no evidence for “cerebral hypoperfusion” in patients with AVM. The distributions of oxygen supply and thus nutritive capillary flow to the cortex surrounding AVMs is almost identical to that in normal cortex. The previously observed “patchy hypoperfusion” in brain tissue surrounding these malformations may therefore correspond overwhelmingly to the “natural” heterogeneity of CBF and is not evidence for steal.

Even in unaffectted human cortex, 7% of the areas have capillary oxygen saturation levels <25% SO2 (ie, below the so-called “lethal threshold” for cerebral venous Po2 of 12 mm Hg), a fact already appreciated previously (eg, see Reference 21). This per se does not indicate tissue hypoxia and is now well explained by recent theories regarding regulation of capillary circulation in the brain, according to which plasmatic capillary flow prevails in this local areas. For further discussion of this phenomenon, we refer to the literature.

Compensating mechanisms, therefore, must counteract the reduced perfusion pressure. Arteriolar dilatation has been...
proven to be one of them but seemingly never to the extent of a maximum CVR reduction. By having shown that SO₂ in the cortex adjacent to AVM never follows alterations of MABP passively, we were able to corroborate these findings. We thus reproduced the results of Young et al., demonstrating that chronic hypotension does not result in “vasomotor paralysis” regardless of whether or not a hyperemic complication subsequently occurs. Their hypothesis of an adaptive autoregulatory displacement (ie, a shift of the autoregulatory curve to the left) seems correct.

An increased capillary density as a structural mechanism of adaption has recently been appreciated. A third mechanism to compensate for a low CPP is a reduced glucose and oxygen metabolism without increased oxygen extraction in the perilesional brain tissue, which has been found in studies with either positron emission tomography or PtO₂ electrodes. Accordingly, our results did not point to a higher than normal oxygen consumption. A fourth mechanism speculated by Hoffman et al. and us lies at the level of capillary regulation itself. Because of the less heterogeneous SO₂ distribution in group A of patients with AVM in contrast to those without AVM, we also hypothesize that erythrocytic capillary recruitment as defined by Kuschinsky and Paulson plays an independent role. Very few scattered hypoxic areas around AVMs not prone to postoperative hyperemic complications might trigger this mechanism, as known from animal experiments.

Figure 3. Regression lines for SO₂ recordings in the cortex during induced elevation of MABP by continuous intravenous infusion of 5 μg/min noradrenaline. All slopes with a significant (P<0.05) regression are shown, which do not represent true autoregulation curves because CBF was not measured directly. SO₂ changes were considered estimates for CBF behavior under the given constant metabolic conditions (see Discussion). A, 18 significant regression lines obtained in patients without AVM (group C). The critical slope for regression lines derived from these data were 0.4% SO₂/mm Hg (mean slope ± 2 SD). B, 18 significant regression lines calculated from recordings in patients with AVM before resection of malformation. None of the regression lines was significantly greater than the critical slope. Autoregulation in all patients was thus classified as intact. Regression lines of 3 patients with subsequent postoperative hyperemic complications (group B) are indicated by dotted lines. C, 16 significant regression lines calculated from recordings in patients with AVM after resection of malformation. None of the regression lines was significantly greater than the critical slope. Autoregulation in all patients was thus classified as intact. Regression lines of 3 patients with postoperative hyperemic complications (group B) are indicated by dotted lines.
We therefore agree with Mast et al that steal should not be defined as cortical ischemia as a consequence of arterial hypotension. Frequent clinical steal phenomena such as progressive focal neurological deficits or impairment of higher cognitive functions are rather a consequence of neuronal deafferentation and diaschisis phenomena in distant or even contralateral regions of the brain.\textsuperscript{36,37,41}

However, severely hypoxic situations in the cortex adjacent to AVMs exist. They are very rare and predominantly encountered in patients prone to postoperative hyperemic complications. We were able to substantiate the existence of such local areas with SO\textsubscript{2} patterns resembling that of “low-flow anoxia” in all patients with a breakthrough, consistent with a previous report.\textsuperscript{42} Because we could not demonstrate vasoparalysis in these patients, exhausted arteriolar regulation is most probably not the single underlying mechanism that leads to drastically reduced oxygen supply in those cortical areas. This is in agreement with other authors\textsuperscript{12–15,36,37} who argue that persistent hemodynamic effects are not primarily responsible. It remains speculative as to which of the above-mentioned other compensating mechanisms are disturbed,\textsuperscript{13} leading to local supply situations indicative for morphological damage.

**Postoperative Breakthrough**

Immediately after the resection of AVMs, a significant increase in cortical capillary SO\textsubscript{2} (ie, a shift of the distributions to the right) takes place in virtually all patients. This can certainly be regarded as flow-related because a hyperemic environment in the surrounding brain tissue—as opposed to the formerly postulated “normalization” of CBF—has already been demonstrated.\textsuperscript{14} The observed patterns in cortical areas of patients without breakthrough correspond to that of reactive hyperemia in the sense that supply exceeds demand. We encountered the highest postoperative SO\textsubscript{2} values in patients with subsequent neurological deteriorations caused by brain swelling and hemorrhage. The same observation was communicated by Young et al.\textsuperscript{14} In further accordance with the results of this group,\textsuperscript{15} we could not find evidence for abolished pressure autoregulation regardless of the occurrence of breakthrough complications.

We conclude that normalized perfusion pressure after AVM resection leads to moderate reactive hyperemia in all patients with uneventful postoperative course because intact feedback mechanisms beyond the myogenic response (ie, metabolic feedback) limit the reperfusion. Because the highest increase in capillary oxygen saturation values measured in the surrounding cortex immediately after resection takes place in cortical areas with evidence for a prior state of severe hypoxia, we confirm the notion of Spetzler et al\textsuperscript{4} that “breakthrough of normal perfusion pressure occurs in an ischemic cortex.” However, vasomotor paralysis is not responsible for this phenomenon. It is much more likely that uncoupling of CBF and metabolism has taken place in those local areas. As a consequence of the lacking metabolic feedback, insufficiently limited hyperperfusion results in a reperfusion injury as described for various other ischemic conditions of the brain. In contrast to Hoffman et al,\textsuperscript{38} who assume that capillary recruitment itself renders the capillary bed vulnerable to normalized perfusion pressure, we are therefore convinced that obviously the lack of recruitment in these areas promotes breakthrough. Structural deficiencies of the capillaries that occur in the process of neovascularization have been observed in an animal model for AVMs and may contribute to the breakdown of the blood-brain barrier.\textsuperscript{45}

All in all, we think that the underlying mechanism for the occurrence of brain swelling and hemorrhage after AVM resection is not as unique to this disease, as it might be inferred from the NPPB theory.

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**References**


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Bernhard Meyer, Carlo Schaller, Christian Frenkel, Bernd Ebeling and Johannes Schramm

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