Effect of Prazosin on Microvascular Perfusion During Middle Cerebral Artery Ligation in the Rat
Mujahid Anwar, Ellen Buchweit-Milton, and Harvey R. Weiss

The purpose of this study was to evaluate the effects of prazosin, an α1-adrenoceptor antagonist, on morphometric indexes of the total and perfused cerebral microvascular bed 1 hour after middle cerebral artery (MCA) ligation in pentobarbital-anesthetized rats. We hypothesized that this agent would prevent catecholamine-induced vasoconstriction in the ischemic brain.

Cerebral blood flow (CBF) was determined with 14C-iodoantipyrine, and the perfused microvascular bed was visualized using fluorescein isothiocyanate-dextran. MCA occlusion did not alter systemic hemodynamic or blood gas parameters. CBF averaged 29 ± 15 (mean ± SD) ml/min/100 g in the MCA-ligated cortex and 49 ± 18 in the other examined brain regions.

Prazosin did not significantly alter these CBF values, averaging 26 ± 14 and 48 ± 10, respectively. There were no significant regional differences in total capillaries/mm² in either group. The percent of the capillaries/mm² perfused (51 ± 6%) was similar in the two groups in all examined regions except the ischemic cortex. In the MCA-ligated cortex, 22 ± 8% of the capillary volume was perfused in comparison with 49 ± 8% in the prazosin-treated group. Prazosin-treated rats had an increased percentage of their microvasculature perfused despite a similarly reduced CBF. Prazosin appeared to reduce diffusion distances in the ischemic cortex. This might be due to its α1-adrenoceptor blocking activity. (Circulation Research 1988;63:27–34)

Experimentally induced stroke results in a significant decrease in cerebral blood flow (CBF) in the affected cortex. 1,2-5 Cerebral metabolic rate may also fall if oxygen extraction does not increase to maintain oxygen consumption. 1,2-6 Oxygen extraction increases during ligation of the middle cerebral artery (MCA). 1 This increased O2 extraction can occur if the tissue oxygen gradient increases, if blood flow through already perfused capillaries increases, or if a greater number of capillaries are perfused.

We have previously shown that, on the average, approximately half of the arteriolar and capillary network of the brain is perfused in barbiturate-anesthetized or conscious rat. 7-10 This reserve of unperfused microvessels is, however, not mobilized in the rat MCA occlusion model. 11 Measurements of the percentage of arterioles and capillaries perfused in the ischemic cortex 20 seconds after fluorescein isothiocyanate (FITC)-dextran injection resulted in a significantly lowered value as compared with the normal contralateral cortex. The cause of this reduction in perfused capillary and arteriolar volume after MCA occlusion may be a consequence of the MCA occlusion itself. However, massive release of catecholamines from brain regions made ischemic by cerebral artery ligation can stimulate adrenoceptors on pial and parenchymal blood vessels, producing vasoconstriction. 12 We hypothesized that prazosin, an α-adrenoceptor, by blocking this effect of catecholamines, might increase CBF and/or increase the number of perfused capillaries and arterioles in the ischemic cortex.

The techniques used in this study have been previously validated in our laboratory to selectively determine morphometric indexes of the perfused and total arteriolar and capillary bed in the brain through comparison of FITC-labeled vessels with alkaline phosphatase-stained preparations of the regional microvascular network. 7 The middle cerebral artery was approached using a modified microsurgical technique of Tamura et al 13 and CBF was measured using 14C-labeled iodoantipyrine. 14 We used these techniques to determine the effects of prazosin, an α1-adrenoceptor antagonist, on the regional CBF and microvascular perfusion in a rat...
subjected to MCA ligation to determine whether prazosin increased flow or the number of perfused microvessels in the ischemic cortex.

Materials and Methods

Adult Long-Evans rats of either sex weighing 300–500 g were used. Right femoral artery and vein catheters were inserted under sodium pentobarbital anesthesia (50 mg/kg ip). The venous catheter was used for the administration of prazosin, FITC-dextran, or $^{14}$C-iodoantipyrine. The arterial catheter was used to measure heart rate and blood pressure and to anaerobically obtain arterial blood samples for analysis of blood gases and pH.

The surgical procedures used to expose and ligate the MCA were modified from those of Tamura et al. A13 An incision was made near the superior and posterior margins of the temporalis muscle. The infratemporal fossa was exposed. A hole was drilled at the junction between the medial wall and the roof of the infratemporal fossa. The position of the skull opening was about 3 mm anterior and 1 mm lateral to the foramen ovale. The MCA was distinguished from its accompanying vein by color and by being straighter and usually having fewer branches. The artery was ligated as close to the base of the skull as possible. In the sham-operated control group, a ligature was placed around the MCA.

Animals were allowed to stabilize for 15 minutes after surgery. Prazosin was administered intravenously as a bolus in two doses of 0.5 mg/kg, 30 minutes apart. Control animals received an equivalent volume of normal saline. Arterial blood pressure was continuously measured using a Statham P23AA transducer (Gould Instruments, Cleveland, Ohio) coupled to the arterial catheter and recorded on a Beckman R-411 recorder (Fullerton, California). An O.2-ml arterial blood sample was withdrawn anaerobically and analyzed for Po$_2$, Pco$_2$, and pH on a blood gas analyzer (BMS model 3, Radiometer America, Westlake, Ohio) prior to the determination of CBF or the injection of FITC-dextran. Regional CBF and perfused and total capillary and arteriolar morphology were determined 1 hour after the administration of prazosin or saline in treated and control animals, respectively.

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We determined CBF using a modified technique of Sakurada et al. After final heart rate, blood pressure, and blood gas determination, $^{14}$C-iodoantipyrine (Amer sham, Arlington Heights, Illinois) was infused into the venous catheter by means of an infusion pump (Sage Instruments, Cambridge, Massachusetts). At the time of the entry of the isotope into the venous circulation, the arterial catheter was cut to a length of 15–20 mm to minimize smearing in the sampling catheter. Timed blood samples were withdrawn from the arterial catheter and collected every 3 seconds in capillary tubes. These samples were collected over a period of 60 seconds at which time the rat was decapitated to terminate perfusion at the moment the last sample was obtained. The brain was frozen in liquid nitrogen for later analysis. While frozen, the brain was cut in the midsagittal plane, and the following regions were dissected: ischemic cortex, contralateral cortex, thalamus, pons, medulla, and cerebellum. Blood and tissue samples were then placed in Soluene (Packard, Downers Grove, Illinois) and 24 hours later in Dimiscint (National Diagnostic, Manville, New Jersey) and agitated. These samples were counted on a Beckman LS-230 liquid scintillation counter. No appreciable quenching was found to occur.

Regional blood flow determinations were made using a computer program based on the equation: $C_i(T) = \kappa R_i/T + C_e e^{-K T - D}$, where $C_i(T)$ equals the tissue concentration of the $^{14}$C-iodoantipyrine at the time of decapitation; $\kappa$ equals the tissue:blood partition coefficient; $C_e$ is the arterial concentration of the tracer; and $t$ equals time. $K$ is defined as follows: $K = mF/W$, where $m$ is a constant related to diffusion (we assume $m = 1$); $F/W$ equals the blood flow per unit mass of tissue. The $\kappa$ value of 0.80 calculated by Sakurada et al. was used.

Regional perfused and total capillary and arteriolar morphology were determined in another group of rats after MCA occlusion and 1 hour after prazosin or saline administration as described previously. After the final determination of heart rate, blood pressure, and arterial blood gas, 150 mg/kg FITC-dextran (70,000 m.w., Sigma Chemical, St. Louis, Missouri) was injected intravenously as a 0.5 ml bolus. Twenty seconds after the injection of FITC-dextran, the animals were killed, and the head was quickly frozen in liquid nitrogen and stored at –70° C until analysis. Brains were exposed midsagittally, and the same regions used for flow determination were isolated and mounted on a microtome specimen holder and coated with embedding medium (O.C.T. Compound, Lab Tek Products, Naperville, Illinois). Two-micron sections were cut on a Sile microtome-cryostat set at –35° C, transferred to glass slides and allowed to dry. Approximately 12 sections were cut for capillaries and 15 for arterioles. Each section was cut 150–200 µm from the previous one.

The slides were photographed on a Zeiss fluorescent microscope equipped for automated photography. A ×40 objective was used to photograph the capillaries, and a ×10 objective was used to photograph the arterioles. The slides were epi-illuminated with violet light from a 100 W halogen source to excite the fluorescence in the FITC-dextran. A barrier filter was placed in the viewing field to allow 495 nm or greater wavelength light through. A second photograph of the same field was taken in normal light, which, together with the viewing coordinates obtained, helped relocate the field.

The slides were then stained for alkaline phosphatase as previously described. The slides were fixed in a sucrose-formalin buffer for 1 minute, were washed twice in distilled water, and were then...
TABLE 1. Effect of 1 Hour of Middle Cerebral Artery (MCA) Occlusion on Hemodynamic and Blood Gas Parameters in Control and Prazosin-Treated Rats

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control Pre 1 hr MCA occlusion</th>
<th>Control Post 1 hr MCA occlusion</th>
<th>Prazosin Pre 1 hr MCA occlusion</th>
<th>Prazosin Post 1 hr MCA occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>123 ± 22</td>
<td>117 ± 22</td>
<td>119 ± 19</td>
<td>85 ± 13†</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>98 ± 16</td>
<td>94 ± 17</td>
<td>89 ± 16</td>
<td>59 ± 8†</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>287 ± 70</td>
<td>277 ± 70</td>
<td>332 ± 59</td>
<td>303 ± 63</td>
</tr>
<tr>
<td>( P_{O_2} ) (mm Hg)</td>
<td>84 ± 15</td>
<td>94 ± 21</td>
<td>91 ± 24</td>
<td>89 ± 13</td>
</tr>
<tr>
<td>( P_{CO_2} ) (mm Hg)</td>
<td>39 ± 4</td>
<td>36 ± 6</td>
<td>37 ± 4</td>
<td>30 ± 8†</td>
</tr>
<tr>
<td>pH</td>
<td>7.40 ± 0.13</td>
<td>7.34 ± 0.12</td>
<td>7.42 ± 0.08</td>
<td>7.47 ± 0.10</td>
</tr>
</tbody>
</table>

*Significantly different from control group value.
†Significantly different from pre MCA occlusion value.

placed in an incubation mixture for 30 minutes at 37° C. The incubation mixture consisted of 3.8 g/l Fast blue RR, 0.5 g/l \( \alpha \)-naphthyl phosphate, 3.8 g/l sodium metaborate, and 1.7 g/l magnesium sulfate. The slides were post-fixed and dried. The field previously photographed for fluorescence was relocated and a new photograph was obtained.

Various stereological determinations were performed, counting each field twice, once for the total and once for the perfused microvasculature. These stereological principles have been reviewed by Weibel and applied to the brain microvasculature. The system used was a Dapple image analyzing device. We placed the slides that were stained for alkaline phosphatase under a microscope, relocating the field previously photographed for fluorescence. The image analyzer was used to evaluate the slides for the total morphometric indexes of the microvasculature. The image was obtained from a Panasonic TV camera attached to the microscope and digitized with the Dapple image analyzer. The programs digitize the raw image by measuring the brightness in 64 gray scale-level steps at each point in a 254×192 array in the picture. The image was automatically edited through the various subroutines in the Dapple system and manually edited with a light pen.

The volume fraction (\( V_v \), in mm\(^3\)/mm\(^3\)) of the microvasculature was determined by dividing the number of test points falling within the profile of a microvessel by the total number of points within the array. The total number of test points was selected so that probable error in \( V_v \) would be less than ±5% for capillaries and ±7.5% for arterioles. The number of capillaries and arterioles/mm\(^2\), \( N_v \), was determined from the number of vessels per unit test area. After the total microvasculature was studied, the perfused portion was obtained from photographs of the fluorescence within the microvasculature. The light pen was used to edit the digitized image for similar measurements of the perfused microvasculature. Average diameter, \( D \), of the microvessels was determined by the measurement of minimum diameter of any vessel cut in transverse section so that the maximum diameter was no more than 1.5 times the minimum. Vessels with an edge-to-edge diameter of less than 11 \( \mu \)m were considered capillaries, and all arterioles with diameters between 19–50 \( \mu \)m were counted. The diameters measured consisted of the lumen and endothelial walls.

Analysis of variance was used to determine the differences between regions (e.g. ischemic and contralateral cortices) and between groups for the various measurements performed. Post hoc multiple comparisons were made using Duncan’s post hoc procedure. All values are expressed as mean±SD unless otherwise specified. A value of \( p < 0.05 \) was accepted as significant.

**Results**

The effect of 1 hour of MCA occlusion on hemodynamic and blood gas parameters in control and prazosin-treated rats is shown in Table 1. MCA occlusion for 1 hour had no significant effect on systolic and diastolic blood pressure, heart rate,
Pao2, and Paco2 and pHa in control animals. Administration of prazosin after MCA occlusion resulted in a significant fall in both systolic and diastolic blood pressure. However, in prazosin-treated animals, the blood pressure did not drop below the lower limit of autoregulation in the rat. Arterial PCO2 was also reduced after prazosin administration. Heart rate, PaO2, and pHa were not affected by prazosin treatment.

Regional CBF determined in seven animals in the MCA ligated group and eight animals in the MCA + prazosin-treated group is shown in Figure 1. Cerebral blood flow averaged 49 ± 18 ml/min/100 g in the nonischemic regions of the MCA-ligated group and 48 ± 10 ml/min/100 g in the prazosin + MCA-ligated group. These values were not significantly different from each other. Occlusion of the MCA resulted in a significant fall in blood flow to the ischemic cortex in comparison with the contralateral cortex and most other regions in both groups of animals. Flow values in the ischemic cortex averaged 28 ± 15 ml/min/100 g in the MCA-ligated group and 26 ± 14 ml/min/100 g in the prazosin + MCA-ligated group. Prazosin administration had no significant effect on blood flow to any of the brain regions studied including the ischemic cortex in comparison with the sham-operated control animals.

The total and perfused arteriolar volume fraction (Vv/mm3) of the different brain regions are shown in Table 2. The total arteriolar volume fractions of all the brain regions were similar in the two groups. Figure 2 shows the perfused arteriolar volume as a percent of the total arteriolar volume in all brain regions. There was a significant decrease in the percent perfused arteriolar volume in the ischemic cortex in comparison with the control group. There was also a minor but statistically significant increase in the percent perfused arteriolar volume in the contralateral cortex in the prazosin-treated animals.

The number of total and perfused arterioles/mm2 of the different brain regions is also shown in Table 2. There were no significant differences in the total number of arterioles/mm2 between the two groups for all brain regions studied except that Na was lower in the cerebellum of the prazosin-treated animals. Figure 3 shows the number of perfused arterioles as a percent of the total number of arterioles/mm2 in all brain regions. There was a significant decrease in the percent perfused arte-
Percent perfused arterioles in the ischemic cortex in comparison with the contralateral cortex in the control animals. There was a small but significant increase in the percent perfused arterioles in the ischemic cortex in prazosin-treated animals in comparison with control animals. Percent perfused arterioles were similar in the two groups in all the other examined brain regions.

The total and perfused capillary volume fraction of the different brain regions is shown in Table 3. There was a significantly lower total capillary volume fraction in the ischemic cortex and cerebellum in the prazosin-treated group than in the MCA-occluded group. No other statistically significant differences in total capillary volume fraction were found. Figure 4 shows the volume fraction of perfused capillaries as a percent of the total tissue volume fraction of capillaries of the different brain regions. There was a significant decrease in the percent perfused volume fraction in the ischemic cortex in comparison with the contralateral cortex in the control animals. There was a significant increase in the percent perfused capillary volume in the ischemic cortex in prazosin-treated animals in comparison with control animals. There was also a minor but statistically significant decrease in percent perfused capillary volume in the contralateral cortex in the prazosin-treated group.

The number of total and perfused capillaries/mm² of the different brain regions is shown in Table 3. There was a significantly decreased total number of capillaries/mm² in the ischemic cortex, cerebellum, and medulla in the prazosin-treated group in comparison with the control group, while other regions were not different. Figure 5 shows the number of perfused capillaries as a percent of the total number of capillaries/mm² of the different brain regions. There was a significant decrease in the percent perfused capillaries in the ischemic cortex in comparison with the contralateral cortex in the control animals. There was a significant increase in the percent perfused capillaries in the ischemic cortex in prazosin-treated animals in comparison with control animals. There was also a small but statistically significant decrease in percent perfused capillaries in the contralateral cortex in the prazosin-treated group.

**Discussion**

Occlusion of the MCA resulted in a significant decrease in blood flow to the ischemic cortex. Tamura et al. reported a decrease in cerebral blood flow that was greatest in the neocortex previously supplied by the MCA and a modest reduction in the

**TABLE 3. Average Total and Perfused Capillary V, (mm²/mm³) and N, (number/mm²) in the Examined Brain Regions of the Middle Cerebral Artery (MCA)-Occluded and MCA-Occluded + Prazosin-Treated Rats**

<table>
<thead>
<tr>
<th></th>
<th>MCA-occluded (n = 7)</th>
<th>MCA-occluded + prazosin (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>V,</td>
<td>N,</td>
</tr>
<tr>
<td>Ischemic total</td>
<td>0.060 ± 0.018</td>
<td>530 ± 129</td>
</tr>
<tr>
<td>Cortex perfused</td>
<td>0.011 ± 0.004</td>
<td>177 ± 68</td>
</tr>
<tr>
<td>Contralateral</td>
<td>0.061 ± 0.031</td>
<td>459 ± 166</td>
</tr>
<tr>
<td>Cortex perfused</td>
<td>0.036 ± 0.032</td>
<td>259 ± 107</td>
</tr>
<tr>
<td>Thalamus total</td>
<td>0.046 ± 0.012</td>
<td>351 ± 117</td>
</tr>
<tr>
<td>Thalamus perfused</td>
<td>0.022 ± 0.012</td>
<td>163 ± 54</td>
</tr>
<tr>
<td>Cerebellum total</td>
<td>0.071 ± 0.026</td>
<td>508 ± 190</td>
</tr>
<tr>
<td>Cerebellum perfused</td>
<td>0.041 ± 0.022</td>
<td>279 ± 102</td>
</tr>
<tr>
<td>Pons total</td>
<td>0.045 ± 0.030</td>
<td>371 ± 40</td>
</tr>
<tr>
<td>Pons perfused</td>
<td>0.017 ± 0.005</td>
<td>211 ± 52</td>
</tr>
<tr>
<td>Medulla total</td>
<td>0.039 ± 0.007</td>
<td>367 ± 42</td>
</tr>
<tr>
<td>Medulla perfused</td>
<td>0.025 ± 0.012</td>
<td>247 ± 71</td>
</tr>
</tbody>
</table>

*Significantly different from corresponding value in MCA-occluded group.
†Significantly different from contralateral cortex in MCA-occluded group.
ipsilateral nucleus accumbens, thalamus, and medial portion of the neostriatum. Our flow decrements were similar to those of Tamura et al with a mean flow of 31 ml/min/100 g in the ischemic cortex in comparison with 55 ml/min/100 g in contralateral cortex after MCA occlusion in barbiturate-anesthetized rats. We have previously shown that MCA occlusion, in comparison to sham-operated animals, resulted in a modest but nonsignificant reduction in blood flow to the thalamus, whereas the levels of blood flow in the ipsilateral and contralateral pons, medulla, and contralateral cortex were not altered. We and other investigators have reported a similar reduction in blood flow and metabolic rate in cats after transorbital ligation of the MCA. This flow deficit in our study was accompanied by a significant reduction in the perfused microvessels in the ischemic cortex.

In the group of rats receiving prazosin during middle cerebral artery ligation, there was a significant fall in arterial blood pressure. However, blood flow to all regions of the brain were similar to those of the untreated animals, indicating intact cerebral autoregulation. Thus, during prazosin treatment, cerebral vascular resistance decreased to maintain cerebral blood flow. There was a significantly lowered arterial PCO2 in the prazosin-treated rats. We are not certain why this occurred. The lower PaCO2 may have somewhat limited the cerebrovascular response to prazosin.

Barbiturate anesthesia tends to lower and cause equal distribution of cerebral blood flow. While it does not alter the average percentage of perfused cerebral microvessels, it tends to reduce regional differences. The reported systemic hemodynamic and blood gas parameters indicated that the animals remained stable and were within a physiologically normal range for barbiturate-anesthetized rats. Barbiturate anesthesia may also have some beneficial effects in a stroke model. However, both experimental groups were studied under the same level of anesthesia. Thus, the effects of the prazosin must be viewed against this constant level of anesthesia. We have previously shown that approximately half of the microvessels of the rat brain are not perfused. This "functional reserve" can be mobilized during asphyxia, severe hypoxia, or hemorrhage. Occlusion of the MCA, on the other hand, resulted in a significant reduction in the perfused microvessels in the ischemic cortex. Others have reported capillary blockage or vasoconstriction during stroke. The vessels in our study, however, were not mechanically blocked because when FITC-dextran was allowed to circulate for 6 minutes almost all of these vessels were perfused. This indicated that blood flow through these vessels was either intermittent or very slow, perhaps because of longer perfusion pathways or slower vasomotion through collateral vessels in the ischemic cortex. The slow perfusion time in some of these vessels indicated that they would contribute very little to the nutritional needs of the tissue.

The techniques utilized in this study to simultaneously determine morphometric indexes of the total and perfused arteriolar and capillary bed in the brain through comparisons of FITC-labeled vessels with the alkaline phosphatase-stained preparation of the regional microvascular network have been...
discussed in detail previously.\textsuperscript{7-9,10} We did note some regional differences between groups in the total capillary but not arteriolar network in certain brain regions. This may have been related to the large variation between rats or seasonal variation in the animals studied.

There is a massive release of catecholamines from brain regions made ischemic by cerebral artery ligation.\textsuperscript{12,20} Both adrenergic and nonadrenergic nerve terminals are found on cerebral capillaries.\textsuperscript{21} The released catecholamines can act on adrenoceptors located in pial and intraparenchymal vessels and reduce flow through vasoconstriction in these microvessels.\textsuperscript{12} This vasoconstriction can increase the extent of ischemic damage and the severity of the resulting neurological deficit. Thus, pharmacological intervention designed to counteract this catecholamine-induced vasoconstriction immediately following stroke may have a protective effect on the ischemic brain. The aim of our study was to test this hypothesis on the role of catecholamine-induced vasoconstriction of the microvessels of the brain made ischemic by MCA occlusion. We utilized prazosin, which is an \textalpha{}-adrenergic antagonist, administered shortly after MCA occlusion to assess its effect on cerebral blood flow and perfused microvessels.

Ligation of the MCA resulted in a significant fall in CBF as well as the number of perfused microvessels. Our results indicated that prazosin did not increase the blood flow to the ischemic cortex. However, prazosin significantly increased the number of perfused microvessels in the ischemic cortex. There were significant increases in the percentage of both the capillary and arteriolar bed perfused in the ischemic cortex. This indicated that stimulation of \textalpha{}-adrenoceptors may limit the number of perfused microvessels in the ischemic cortex of the barbiturate-anesthetized rat. Similar results have been reported with subarachnoid hemorrhage. Delgado et al.\textsuperscript{22} have reported that subarachnoid hemorrhage resulted in a decreased cerebral blood flow. This also appeared to be related to catecholamine-induced vasoconstriction since lesioning of the ascending adrenergic system prevented this reduction in CBF.

Prazosin had no significant effect either on the number of perfused cerebral capillaries or on cerebral blood flow in any of the nonischemic brain regions studied. Since arterial pressure was lowered by prazosin, it is likely that there was some cerebral arteriolar vasodilation in order to maintain blood flow. There was also a tendency for perfusion of cerebral arterioles to increase with prazosin. This was significant in the contralateral cortex and cerebellum. The somewhat lower arterial P\textsubscript{co\textsubscript{2}} may have limited the capillary response to prazosin in the ischemic cortex. However, hemorrhage, which lowered cerebral flow to a similar extent with accompanying hypocapnia, led to an increase in the percentage of the capillary bed perfused.\textsuperscript{10}

The effect of adrenergic receptor blockade has been studied in patients with stroke by Meyer et al.\textsuperscript{23} and in cats after MCA occlusion by Little et al.\textsuperscript{24} Little et al.\textsuperscript{24} noted a protective effect of propranolol on ischemic brain tissue after 6 hours of partial ischemia. However, in a later study these authors were unable to find a reduction in infarct size in propranolol treated animals. Meyer et al.\textsuperscript{23} used a combination of propranolol and phenoxybenzamine to block both \textalpha{}- and \beta{}-adrenoceptors in patients with stroke. They found an increase in the neurological deficit in four of their patients and no improvement in outcome in other patients receiving this therapy. The unfavorable outcome in their study may be due to the fact that they started therapy 1–38 days after the onset of stroke. Robinson et al.\textsuperscript{20} have shown that after MCA occlusion in rats a widespread depletion of brain catecholamines occurred after 12 hours of surgery with levels gradually returning to normal by 30–40 days postsurgery. Adrenergic blockade at a time when the brain catecholamine levels are low is not likely to be efficacious.

We have found that MCA ligation resulted in a decrease in CBF and the number of perfused microvessels. Prazosin increased the number of perfused microvessels in the ischemic cortex of an MCA ligated barbiturate-anesthetized rat with no significant effect on any other brain region. This effect should reduce the diffusion distances for oxygen within the ischemic cortex. This effect of prazosin is most likely related to its \textalpha{}-adrenoceptor blocking properties preventing vasoconstriction caused by ischemia-induced release of catecholamines. In the present study, we have shown that this effect can occur during the first hour of ischemia, but have not determined how long this effect will continue.

References

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**KEY WORDS** cerebral blood flow • cerebral capillary density • stroke • a-adrenoceptors
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