Segmental vascular responses to acute hypertension in cerebrum and brain stem

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FARACI, FRANK M., WILLIAM G. MAYHAN, AND DONALD D. HEISTAD. *Segmental vascular responses to acute hypertension in cerebrum and brain stem.* Am. J. Physiol. 252 (Heart Circ. Physiol. 21): H738–H742, 1987.—The goal of this study was to examine hemodynamic mechanisms that contribute to regional differences in autoregulation during acute hypertension. We measured blood flow (microspheres) and pressure in pial arteries (~160 μm) of anesthetized cats and calculated resistance of large and small vessels in cerebrum and brain stem. Moderate elevation of aortic pressure increased resistance of both large and small vessels in cerebrum but only small vessels in brain stem. During severe hypertension, resistance of both large and small vessels in cerebrum decreased and blood flow increased markedly. In contrast, in the brain stem large artery resistance did not change, small vessel resistance increased, and blood flow increased only modestly during severe hypertension. Pial artery pressure was 20 mmHg higher in brain stem than cerebrum during control conditions and 30–50 mmHg higher during moderate and severe hypertension. We conclude that resistance of large arteries is less and thus pial artery pressure is higher in brain stem than cerebrum under control conditions. More effective autoregulation in the brain stem than cerebrum during severe hypertension is due to greater resistance of small, not large, cerebral vessels.

segmental resistance; cerebral circulation; pial artery pressure; cat

THE CEREBRAL CIRCULATION is characterized by very effective autoregulation of blood flow during changes in perfusion pressure (2, 9, 12, 14). During moderate increases in aortic pressure, cerebral vessels constrict and blood flow throughout the various brain regions is maintained near normal levels (2, 6). In contrast, there are important regional differences in autoregulation during severe hypertension (2). For example, during severe hypertension autoregulatory capacity is exceeded at a lower level of pressure in the cerebrum than in the brain stem (2).

Mechanisms that account for these regional differences in autoregulation are not known. Differences between the brain stem and cerebrum in responsiveness to acute hypertension apparently are not due to regional differences in the ratio of gray to white matter, vasoconstrictor or vasodilator capacity, or amount of sympathetic innervation to vessels that supply these regions (2).

To examine hemodynamic mechanisms that contribute to regional differences in autoregulation in the brain, we determined segmental vascular responses to moderate and severe increases in aortic pressure in the cerebrum and brain stem. In both the cerebrum (1, 9, 12, 16) and the brain stem (7), resistance of large arteries is a significant portion of total vascular resistance. We considered two possible mechanisms that might account for more effective autoregulation in the brain stem.

One possibility was that, during increases in systemic pressure, large artery resistance might increase more in the brain stem than cerebrum and attenuate increases in pial artery pressure. Attenuation of increases in pial artery pressure could extend the upper limit of autoregulation in the brain stem compared with the cerebrum, even if the autoregulatory response of small vessels were similar in the two regions.

An alternative hypothesis was that the autoregulatory response of small vessels is different in the two regions of the brain. Recent measurements indicate that during normotension pial artery pressure (in similar-sized vessels) is higher in brain stem than cerebrum (13). Chronic exposure to a higher arteriolar pressure could result in altered vascular responses. Thus we considered the possibility that small vessels in the brain stem autoregulate more effectively than small vessels in the cerebrum.

METHODS

Animal preparation. Nineteen cats (1.9–3.0 kg) were used in these experiments. Cats were anesthetized with pentobarbital sodium (35 mg/kg ip) supplemented at 5–10 $mg \cdot kg^{-1} \cdot h^{-1}$ as needed. After a ventral midline incision, the trachea was cannulated and animals were ventilated with air and supplemental O_2. Paralysis of skeletal muscle was produced with gallamine triethiodide (5 mg/kg). A catheter was inserted into a femoral artery and advanced until the tip was in the thoracic aorta for pressure measurement. A femoral vein was cannulated for infusion of drugs. Catheters were placed in both axillary arteries for withdrawal of reference blood samples during microsphere injection and into the left atrial appendage for injection of microspheres. A ligature was placed around the descending thoracic aorta below the tip of the arterial catheter for partial aortic occlusion (see *Experimental protocol*). Rectal temperature was continually monitored with a telethermometer and was maintained between 37 and 38°C with a heating pad.

Measurement of cerebral blood flow. Cerebral blood flow

was measured using radioactive microspheres (15 μm) labeled with either ^{46}Sc, ^{95}Nb, ^{85}Sr, ^{113}Sn, or ^{141}Ce. After vigorous shaking for several minutes, 0.4–1.6 $\times$ 10^6 microspheres were injected slowly (15–20 s) into the left atrium, followed by a saline flush. Beginning 15 s before injection of microspheres and continuing for 60 s after the saline flush, reference arterial blood samples were withdrawn from both axillary arteries at 1.03 ml/min.

At the end of the experiment, the animal was killed with an intravenous injection of KCl, and the brain was removed and placed in buffered Formalin for 1–3 days before dissection into regional samples. Tissue samples and reference arterial blood samples were counted using a 3-in. NaI well-type gamma counter (Beckman 300). Isotope separation was performed using standard techniques (11). Cerebral blood flow (CBF; ml·min^{-1}·100 g^{-1}) was calculated as $CBF = (C_t \times 100 \times Q_r)/C_r$, where Q_r is the reference sample flow rate and C_t and C_r are counts in tissue and reference samples, respectively.

Measurement of pial artery pressure and venous pressure. After insertion of all catheters, the animal was placed in a head holder. A craniotomy was made to expose vessels that supply either the cerebrum or the brain stem as described previously (1, 7). In 11 cats, we studied vessels that supply the cerebrum. In eight cats, we studied vessels that supply the brain stem.

Among animals in which we studied the cerebrum, the scalp and temporalis muscle were removed on the left side. With the use of an air-cooled dental drill, a craniotomy was made over the parietal cortex. A dam made of bone wax and equipped with inlet and outlet lines was constructed around the craniotomy. Artificial cerebrospinal fluid (CSF) was equilibrated with gas mixtures, warmed to 37°C, and continuously suffused over the exposed portion of brain. The dura was incised with ophthalmic scissors to expose pial vessels over the cerebrum. A small burr hole was made over the midline, and a 24-gauge catheter was inserted into the dorsal sagittal sinus to measure venous pressure in the cerebrum.

Among cats in which we studied the brain stem, the larynx and esophagus were retracted laterally and rostrally, and the muscle covering the basioccipital bone was removed. A craniotomy was made in the base of the skull between the tympanic bullae using an air-cooled dental drill. With the use of inlet and outlet lines, artificial CSF was continually suffused over the exposed portion of brain stem. The dura was incised with ophthalmic scissors to expose the ventral medulla. In both groups of cats, CSF sampled from the craniotomy had a P_{CO_2} of 42 ± 1 mmHg, a P_{O_2} of 67 ± 4 mmHg, and a pH of 7.33 ± 0.02.

Pial artery pressure (PAP) was measured using sharpened micropipettes (2–5 μm tip diameter) filled with 1.5 M NaCl and coupled to a servo-null pressure-measuring device (model 4A, Instruments for Physiology and Medicine). The tip of the micropipette was inserted into the lumen of pial arteries that supply the cerebrum or medulla using a Leitz micromanipulator. Vessels were observed using a trinocular stereomicroscope (Wild) equipped with a television camera coupled to a video monitor and video recorder. Vessel diameter was measured using either an image analyzer or video monitor and stage micrometer.

Experimental protocol. In one group of animals, we measured PAP and venous pressure (sagittal sinus) in the cerebrum. In the second group of animals, we measured PAP and venous pressure in a large surface vein (268 ± 58 μm) on the ventral medulla. Similar-sized pial arteries were selected in cerebrum and brain stem.

Moderate increases in systemic pressure in the upper portion of the body were produced by partial aortic occlusion. After release of partial aortic occlusion and before induction of severe hypertension, systemic pressure returned to control levels. Severe increases in systemic pressure were produced using aortic occlusion in combination with intravenous infusion of norepinephrine (5–10 μg/min). Regional CBF and arterial blood gases were measured during normotension, after 1–2 min of moderate hypertension, and after 1–2 min of severe hypertension.

Large artery resistance was calculated as (aortic pressure − PAP)/blood flow to either the cerebrum or medulla. Small vessel resistance was calculated as (PAP − venous pressure)/blood flow. Thus small vessel resistance includes small pial arteries and arterioles, capillaries, and venules.

Statistics. Statistical analysis was performed using paired *t* tests to compare control and intervention values. An unpaired *t* test was used to compare values between different groups of animals (brain stem vs. cerebrum). Bonferroni correction was used for multiple comparisons. A P value <0.05 was considered significant.

RESULTS

Control conditions. During control conditions, blood flow to the cerebrum and brain stem was similar in the two groups of animals (Table 1). Pial artery diameter was 164 ± 10 in the cerebrum and 161 ± 11 (SE) μm in the brain stem, but PAP was 20 mmHg higher in the brain stem than the cerebrum (Table 1). Large artery resistance (vessels >~160 μm) was 47 ± 4% of total resistance in cerebrum and only 25 ± 3% of total resistance in brain stem ($P < 0.05$ vs. cerebrum). Thus resistance of large arteries is a significant portion of total resistance in both regions of the brain, but the relative contribution to total resistance is greater in large arteries that supply the cerebrum.

Responses to moderate hypertension. During moderate hypertension, systemic pressure was increased by ~40 mmHg in both groups of animals (Fig. 1). Total vascular resistance increased, and blood flow to both the cerebrum and brain stem was maintained near control levels (Table 1).

In the cerebrum, resistance of both large and small vessels increased during moderate hypertension, but the increase in resistance was greater in small vessels (Fig. 2).

In the brain stem, large artery resistance decreased significantly during moderate hypertension (Fig. 2). In contrast to large arteries, resistance of small vessels in the brain stem increased during moderate hypertension. Thus, during moderate hypertension, large artery resist-

TABLE 1. *Effects of acute hypertension on cerebral blood flow and segmental resistances in cerebrum and brain stem*

	Cerebrum			Brain Stem		
	Control	Moderate hypertension	Severe hypertension	Control	Moderate hypertension	Severe hypertension
Blood flow, ml·min^{-1}·100 g^{-1}	30±2	34±2	101±18*	27±4	31±3	54±9*†
Aortic pressure, mmHg	89±6	133±4*	200±5*	93±7	134±5*	204±5*
Pial artery pressure, mmHg	51±7	81±5*	117±5*	71±6†	113±5*†	169±6*†
Venous pressure, mmHg	4±1	5±1	17±4*	3±1	4±1	8±1*†
Resistance, mmHg·ml^{-1}·min·100 g						
Total	3.0±0.2	4.0±0.3*	2.2±0.3	3.9±0.5	4.6±0.5*	4.9±0.8*†
Large arteries	1.4±0.1	1.6±0.1*	0.9±0.1*	1.0±0.1†	0.7±0.1*†	1.0±0.2
Small vessels	1.6±0.2	2.4±0.2*	1.3±0.2	2.9±0.4†	3.9±0.4*†	3.9±0.6*†
Arterial P_{CO_2}, mmHg	31±1	32±1	33±2	30±1	30±1	29±1
Arterial P_{O_2}, mmHg	151±10	145±13	148±14	152±15	156±15	172±10
Arterial pH	7.35±0.01	7.32±0.02	7.27±0.02	7.36±0.02	7.35±0.02	7.35±0.02
n	11	11	8	8	8	8

Values are means ± SE; *n*, no. of cats. * $P < 0.05$ vs. control. † $P < 0.05$, brain stem vs. cerebrum.

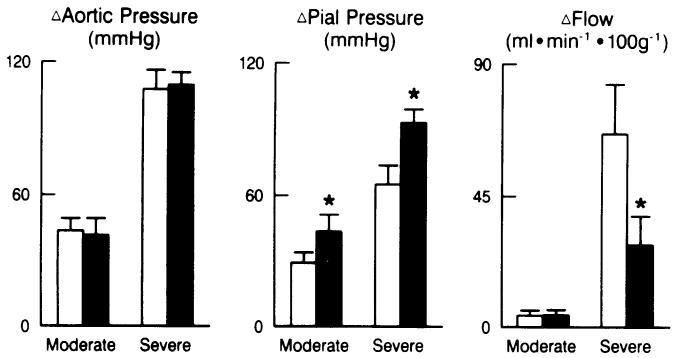

FIG. 1. Changes (△) in aortic pressure, pial artery pressure, and blood flow in the cerebrum (*open bars*) and brain stem (*closed bars*) during moderate and severe hypertension. Values are means ± SE. * $P < 0.05$, brain stem vs. cerebrum.

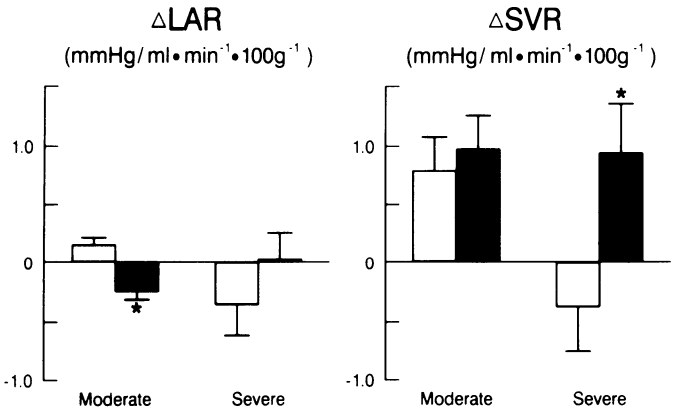

FIG. 2. Changes in large artery (ΔLAR) and small vessel resistance (ΔSVR) in cerebrum (*open bars*) and brain stem (*closed bars*) during moderate and severe hypertension. Values are means ± SE. * $P < 0.05$, brain stem vs. cerebrum.

ance is lower and small vessel resistance is higher in the brain stem than in the cerebrum (Table 1).

Responses to severe hypertension. The autoregulatory capacity of vessels that supply the cerebrum was exceeded during severe hypertension. Resistance of large arteries decreased significantly and small vessel resistance tended to decrease during severe hypertension (Table 1). PAP on the cerebrum was more than twice the normal level. Cerebral venous pressure also increased significantly.

In contrast to the cerebrum, the autoregulatory capacity of brain stem vessels was not exceeded during severe hypertension. Resistance of large arteries was maintained at control levels and small vessel resistance increased during severe hypertension (Fig. 2). Consequently, the change in blood flow during severe hypertension was less in brain stem than in cerebrum (Fig. 1). PAP increased more in the brain stem than in the cerebrum (Fig. 1). Venous pressure increased during severe hypertension, but the increase was less than in the cerebrum (Table 1).

Thus, during severe hypertension, resistance of large and small vessels in cerebrum failed to increase. In contrast, in the brain stem large artery resistance was not changed and small vessel resistance increased.

DISCUSSION

There are three major new findings in the present study. First, under control conditions, resistance of large arteries is a more important determinant of blood flow in the cerebrum than in the brain stem. Second, moderate elevation of arterial pressure, within the range of autoregulation, increases resistance of both large and small vessels in the cerebrum but exclusively small vessels in the brain stem. Third, resistance of large and small vessels in the cerebrum decreases during severe hypertension. In contrast, resistance of small vessels increases in the brain stem during severe hypertension.

Consideration of methods. In this study we used pentobarbital for anesthesia and gallamine triethiodide for paralysis. In previous studies, we observed a similar pattern of regional differences in autoregulation during severe hypertension in animals that received different combinations of anesthesia and paralytic agents (chloralose with gallamine and chloralose-urethan with decamethonium bromide) (2, 10). Thus vascular responses to acute hypertension are comparable under different anesthesic regimens.

Norepinephrine was used to induce severe hypertension in this study. Intravascular infusion of norepinephrine has no direct effect on diameter of cerebral vessels (12) and does not affect cerebral blood flow or resistance of large or small cerebral vessels (16) when blood pressure

is maintained constant. In addition, the pattern of changes in regional cerebral blood flow during severe hypertension induced by norepinephrine is similar to those induced by angiotensin alone and by aortic occlusion alone (2). Thus, in these studies, norepinephrine appears to be an appropriate agent to induce acute hypertension.

We have previously measured pial artery pressure and cerebral blood flow and examined the regulation of segmental resistance in the cerebrum (1, 16, 17) and the brain stem (7). We have demonstrated that blood flow to the region within the craniotomy responds normally to vasoactive stimuli and that insertion of a micropipette into a vessel does not impair the response of the region supplied by that vessel (1, 7, 17).

In this study we calculated resistance of large and small vessels from values for blood flow to the entire cerebrum or medulla and pressure in a single pial artery. This approach (using a global measurement of blood flow and a local measurement of pressure) could reduce the precision of our calculation of segmental resistance. We have previously measured blood flow to the region perfused by the artery in which pressure was measured in both the cerebrum and brain stem (7, 17). Blood flow to this smaller region and the remainder of the cerebrum or medulla was similar under a variety of conditions (1, 7, 17). Thus we suggest that this method provides a valid estimate of segmental resistance in both the cerebrum and brain stem.

Small vessel resistance was calculated from the decrease in pressure from pial artery to vein divided by blood flow. Resistance of this segment includes the effects of both small precapillary vessels and postcapillary vessels, so that changes in resistance in either of these vascular segments may contribute to changes in small vessel resistance. We measured venous pressure for the cerebrum in the sagittal sinus and for the brain stem in large pial veins on the surface of the ventral medulla. Values for venous pressure were used in the calculation of resistance of small vessels. If venous pressure had been measured in a pial vein on the cerebrum that was similar in size to that on the brain stem, the value for venous pressure that we measured might have been higher because these veins are smaller than the sagittal sinus and they are upstream from the sinus. If the increase in venous pressure in the cerebrum were greater than the increase in pressure that we measured in the sagittal sinus, the decrease in small vessel resistance during severe hypertension would be even greater than calculated. Thus measurement of pressure in different-sized veins in cerebrum and brain stem would not alter our conclusions about responses of small vessels during hypertension.

Segmental resistance under control conditions. Pressure in pial arteries ~160 μm in diameter on the cerebrum averaged 55% of aortic pressure in this study. This finding indicates that almost half of total resistance in the circulation to the cerebrum resides in large arteries >160 μm. In similar-sized arteries on the brain stem, pial artery pressure was higher than in the cerebrum, and resistance of large arteries was only 25% of total resistance. These measurements suggest important regional differences in the distribution of vascular resistance between large and small vessels in the cerebral circulation. Both the relative caliber and the length of large arteries upstream from the point of measurement of microvascular pressure may contribute to differences in large artery resistance in cerebrum and brain stem.

Segmental vascular responses to moderate hypertension. When aortic pressure was increased from ~90 to 130 mmHg, both large and small vessels that supply the cerebrum constricted and contributed to the increase in total resistance. Kontos et al. (12) have emphasized the contribution of large arteries to autoregulation of blood flow to cerebrum during somewhat greater increases in aortic pressure.

In the brain stem circulation, resistance of large arteries decreased during moderate hypertension, which indicates that this vascular segment dilated passively in response to the increase in pressure. Constriction of small vessels in the brain stem accounted for the entire increase in vascular resistance. Our initial hypothesis was that large arteries in the brain stem constrict in response to increases in systemic pressure and thus attenuate increases in arteriolar pressure. Instead, passive dilatation of large arteries resulted in greater transmission of pressure to the pial circulation of the brain stem. Thus, with the same increase in aortic pressure, pial artery pressure increased more in the brain stem than in the cerebrum.

Segmental vascular responses to severe hypertension. During severe hypertension, PAP was 50 mmHg higher in the brain stem than in the cerebrum. These results suggest that attenuation of increases in microvascular pressure by constriction of large arteries is not a mechanism that accounts for more effective autoregulation in the brain stem during acute hypertension.

It is unlikely that neural mechanisms could account for regional differences in autoregulation under the conditions of these studies. Activation of sympathetic nerves attenuates increases in blood flow during acute hypertension (6, 10). If sympathetic tone were withdrawn during severe hypertension, predominantly in the cerebrum, then increases in blood flow could be greater to the cerebrum than to the brain stem. However, there appears to be little if any resting tone of sympathetic nerves on cerebral vessels (10). The alternative neural mechanism, activation of a dilator pathway to the cerebrum, seems unlikely but cannot be excluded.

One mechanism that might contribute to regional variations in autoregulation is regional differences in myogenic responses of cerebral vessels to increases in pressure. Myogenic responses have been observed in isolated cerebral vessels (3) and in pial arteries on the cerebrum (5, 18). We are not aware of any data that suggest that there are regional differences in myogenic responses of blood vessels in the brain. We speculate that myogenic mechanisms may be more effective in small vessels in the brain stem, which constrict during severe hypertension, than in small vessels of the cerebrum, which dilated passively in response to the same increase in systemic pressure.

Metabolic mechanisms appear to play an important role in autoregulatory responses of cerebral vessels (19). Regional differences in metabolism have been observed during acute hypotension (15). It is possible that regional differences in metabolism may contribute to heterogenous changes in cerebral blood flow during acute hypertension.

A third mechanism that may account for regional differences in autoregulation relates to the vasomotor tone of small vessels in the brain stem. Small vessel resistance is greater in the brain stem than the cerebrum under control conditions, which suggests that these vessels are constricted and have smaller diameters compared with small vessels in the cerebrum, or that there are fewer vessels in the brain stem. Considering the first possibility, the law of LaPlace (wall tension = transmural pressure × radius) predicts that, with a smaller resting radius, a smaller increase in tension is required for a small vessel in the brain stem to withstand the same increase in pressure. If small vessels in the cerebrum have a greater resting diameter, they would have to constrict more vigorously in response to the same increase in pressure to maintain normal levels of blood flow. A similar difference in resting vasomotor tone has been proposed to explain differences in autoregulation in the subendocardium and subepicardium during acute hypertension (4). The second possibility, that there are fewer vessels in the brain stem, seems unlikely because maximal dilator capacity is not impaired (2).

Small vessels are exposed to higher levels of arteriolar pressure under normal conditions in the brain stem than in the cerebrum, and thus vessels in the brain stem may be hypertrophied compared with vessels in the cerebrum. Such a structural change would enhance the ability of the vessel to constrict, but also would impair its ability to dilate if the hypertrophy encroached on the lumen (8). Hypertrophy with encroachment on the vessel lumen does not seem likely, because dilator responses to hypercapnia are similar in cerebrum and brain stem (2).

Functional implications. The available data support our initial hypothesis that chronic elevation of arteriolar pressure may lead to altered autoregulatory responses of small vessels in the brain stem. As discussed above, we speculate that an increase in smooth muscle mass in vessels of the brain stem may occur but may not encroach on the vessel lumen. Such nonencroaching hypertrophy may allow selective increases in effectiveness of autoregulation during increases in arterial pressure, by facilitating vasoconstriction, without impairment of vasodilator responses. Our data indicate that small vessels in the brain stem autoregulate more effectively than small vessels in the cerebrum during acute hypertension. More effective autoregulation in the brain stem appears to be a mechanism that protects the blood-brain barrier from disruption during acute hypertension (13).

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REFERENCES

1. BAUMBACH, G. L., AND D. D. HEISTAD. Effects of sympathetic stimulation and changes in arterial pressure on segmental resistance of cerebral vessels in rabbits and cats. *Circ. Res.* 52: 527–533, 1983.
2. BAUMBACH, G. L., AND D. D. HEISTAD. Heterogeneity of brain blood flow and permeability during acute hypertension. *Am. J. Physiol.* 249 (*Heart Circ. Physiol.* 18): H629–H637, 1985.
3. BEVAN, J. A., AND J. J. HWA. Myogenic tone and cerebral vascular autoregulation: the role of a stretch-dependent mechanism. *Ann. Biomed. Eng.* 13: 281–286, 1985.
4. BOATWRIGHT, R. B., H. F. DOWNEY, F. A. BASHOUR, AND G. J. CRYSTAL. Transmural variations in autoregulation of coronary blood flow in hyperperfused canine myocardium. *Circ. Res.* 47: 599–609, 1980.
5. BOHLEN, H. G., AND S. L. HARPER. Evidence of myogenic vascular control in the rat cerebral cortex. *Circ. Res.* 55: 554–559, 1984.
6. BUSIJA, D. W., D. D. HEISTAD, AND M. L. MARCUS. Effects of sympathetic nerves on cerebral vessels during acute, moderate increases in arterial pressure in dogs and cats. *Circ. Res.* 46: 696–702, 1980.
7. FARACI, F. M., D. D. HEISTAD, AND W. G. MAYHAN. Role of large arteries in regulation of blood flow to brain stem in cats. *J. Physiol. Lond.* In press.
8. FOLKOW, B. Physiological aspects of primary hypertension. *Physiol. Rev.* 62: 347–504, 1982.
9. HARPER, S. L., H. G. BOHLEN, AND M. H. RUBIN. Arterial and microvascular contributions to cerebral cortical autoregulation in rats. *Am. J. Physiol.* 246 (*Heart Circ. Physiol.* 15): H17–H24, 1984.
10. HEISTAD, D. D., AND M. L. MARCUS. Effect of sympathetic stimulation on permeability of the blood-brain barrier to albumin during acute hypertension in cats. *Circ. Res.* 45: 331–338, 1979.
11. HEYMANN, M. A., B. D. PAYNE, J. I. E. HOFFMAN, AND A. M. RUDOLPH. Blood flow measurements with radionuclide-labeled particles. *Prog. Cardiovasc. Dis.* 20: 55–70, 1977.
12. KONTOS, H. A., E. P. WEI, R. M. NAVARI, J. E. LEVASSEUR, W. I. ROSENBLUM, AND J. L. PATTERSON, JR. Responses of cerebral arteries and arterioles to acute hypotension and hypertension. *Am. J. Physiol.* 234 (*Heart Circ. Physiol.* 3): H371–H383, 1978.
13. MAYHAN, W. G., F. M. FARACI, AND D. D. HEISTAD. Disruption of the blood-brain barrier in the cerebrum and brain stem during acute hypertension. *Am. J. Physiol.* 251 (*Heart Circ. Physiol.* 20): H1171–H1175, 1986.
14. MUELLER, S. M., D. D. HEISTAD, AND M. L. MARCUS. Total and regional cerebral blood flow during hypotension, hypertension, and hypocapnia. *Circ. Res.* 41: 350–356, 1977.
15. SAVAKI, H. E., H. MACPHERSON, AND J. MCCULLOCH. Alterations in local cerebral glucose utilization during hemorrhagic hypotension in the rat. *Circ. Res.* 50: 633–644, 1982.
16. TAMAKI, K., AND D. D. HEISTAD. Response of large and small cerebral arteries to sympathetic stimulation during acute hypertension. *Hypertension Dallas* 8: 911–917, 1986.
17. TAMAKI, K., W. G. MAYHAN, AND D. D. HEISTAD. Effects of vasodilator stimuli on resistance of large and small cerebral vessels. *Am. J. Physiol.* 251 (*Heart Circ. Physiol.* 20): H1176–H1182, 1986.
18. WEI, E. P., AND H. A. KONTOS. Increased venous pressure causes myogenic constriction of cerebral arterioles during local hyperoxia. *Circ. Res.* 55: 249–252, 1984.
19. WEI, E. P., AND H. A. KONTOS. Responses of cerebral arterioles to increased venous pressure. *Am. J. Physiol.* 243 (*Heart Circ. Physiol.* 12): H442–H447, 1982.