Effect of Chronic Hypertension on Acute Hypertensive Disruption of the Blood-Brain Barrier in Rats

ANDREW H. WERBER AND MARYPAT C. FITCH-BURKE

SUMMARY The effect of chronic hypertension on acute hypertensive disruption of the blood-brain barrier has been studied in only two models of hypertension, with inconsistent results. The purpose of this study was to reinvestigate whether chronic hypertension has a consistent effect on acute hypertensive disruption of the blood-brain barrier and to determine whether one of the previously studied models has an unusual response to chronic hypertension. We studied four rat models of chronic hypertension: spontaneously hypertensive rats (SHR), two-kidney, 1 clip Goldblatt rats (2K1C), rats treated with deoxycorticosterone acetate (DOCA) and NaCl, Dahl salt-sensitive rats fed a high salt diet, and two groups of normotensive controls: Wistar-Kyoto rats (WKY) and Dahl salt-sensitive rats fed a low salt diet. We caused acute hypertension in some rats with the use of bicuculline (1.2 mg/kg) and aortic occlusion. Rats without acute hypertension served as controls. Blood-brain barrier disruption was quantitated using the brain/blood ratio of $^{125}$I-labeled albumin. Acute hypertensive disruption was less in SHR, rats treated with DOCA-NaCl, and Dahl salt-sensitive rats fed a high salt diet, but not in 2K1C rats, as compared with normotensive controls. Acute hypertensive disruption was greater in Dahl salt-sensitive rats fed a low salt diet than in WKY. A series of control WKY, SHR, rats treated with DOCA-NaCl, 2K1C rats, and Dahl salt-sensitive rats fed low or high salt diets, but not subjected to acute hypertension, were also studied. Brain/blood $^{125}$I-albumin ratios were significantly less in these control rats not subjected to acute hypertension than in rats subjected to acute hypertension. In addition, the brain/blood $^{125}$I-albumin ratios did not differ among the groups of control rats not subjected to acute hypertension. The differences in acute hypertensive disruption between groups could not be accounted for by the increase in blood pressure, rate of rise of blood pressure, clearance of $^{125}$I-albumin from the blood, blood gas values, or pH.

We conclude that 1) chronic hypertension reduces the susceptibility of the blood-brain barrier to acute hypertensive disruption, 2) 2K1C rats have an anomalous response to acute hypertensive disruption, and 3) because the degree of acute hypertensive disruption differed between two strains of normotensive rats fed different diets, there may be either a genetic influence or a dietary influence on the susceptibility of the blood-brain barrier to acute hypertensive disruption. (Hypertension 12: 549-555, 1988)

KEY WORDS • blood-brain barrier • acute hypertension • genetic hypertension • renal hypertension • DOCA-salt hypertension

DISRUPTION of the blood-brain barrier during acute increases in blood pressure may be an important event in the pathogenesis of hypertensive encephalopathy in humans and experimental hypertensive stroke.1,2 Hypertensive disruption of the blood-brain barrier is thought to be the result of increased tension (and, perhaps, stress) on blood vessels.3 Because cerebral blood vessels undergo hypertrophy in spontaneously hypertensive rats (SHR),4-6 the change in arteriolar stress, and thus disruption of the blood-brain barrier, during acute hypertension would be expected to be less in SHR than in normotensive Wistar-Kyoto rats (WKY). It has been demonstrated that the blood-brain barrier of SHR is less susceptible to hypertensive disruption.3,7 Whether cerebral vascular hypertrophy is the cause of this protective effect of chronic hypertension on the blood-brain barrier has not been established.

Since hypertrophy of blood vessels may occur in a number of models of experimental hypertension,8 it seemed likely that other models of chronic hyper-
tension would show reduced susceptibility of the blood-brain barrier to acute hypertensive disruption. The susceptibility of the blood-brain barrier to acute hypertensive disruption has been studied in one other model of chronic hypertension—the two-kidney, one clip (2K1C) Goldblatt model. In these studies, the susceptibility of the blood-brain barrier to hypertensive disruption was not reduced in the animals with chronic hypertension. Thus, the effect of chronic hypertension on the susceptibility of the blood-brain barrier to acute hypertensive disruption is unclear. To determine whether chronic hypertension has a consistent effect on the susceptibility of the blood-brain barrier to disruption, we studied the susceptibility of the blood-brain barrier to acute hypertensive disruption in four models of chronic hypertension.

Materials and Methods

Animals

Experiments were performed on male SHR and normotensive WKY (Taconic Farms, Germantown, NY, USA) and male Dahl salt-sensitive rats (DS) obtained from Brookhaven National Laboratories (Upton, NY, USA). Rats were housed in temperature-controlled, light-cycled quarters, with food and water available ad libitum. Rats were fed standard rat chow (Wayne Lab Blox, Chicago, IL, USA; 24% protein, 0.99% KCl; or Purina rat chow, St. Louis, MO, USA; 23% protein, 0.99% KCl) and given tap water unless otherwise noted. All procedures using animals followed institutional guidelines. The mean ages (in weeks) of the rats subjected to acute hypertension were 17 ± 2 (SEM) in 10 2K1C rats, 14 ± 1 in 8 DS fed a high salt diet, 17 ± 2 in 10 DS fed a low salt diet, 13 ± 1 in 7 rats treated with deoxycorticosterone acetate (DOCA) and NaCl, 17 ± 2 in 10 SHR, and 18 ± 2 in 10 WKY. There were no significant age differences (p > 0.05) among these groups. The ages of the rats not subjected to acute hypertension were 19 ± 2 in 5 2K1C rats, 17 ± 3 in 5 DS fed a high salt diet, 15 ± 1 in 5 DS fed a low salt diet, 14 ± 1 in 3 DOCA-NaCl rats, 17 ± 2 in 6 SHR, and 19 ± 4 in 5 WKY. There were no significant age differences (p > 0.05) among the groups of hypertensive rats.

Production of Chronic Hypertension

At about 8 weeks of age, 2K1C Goldblatt hypertension was produced in WKY by constriction of the left renal artery, using a silver clip as described by Brooks et al. A steroid-dependent hypertension (DOCA and NaCl) was produced in 6-week-old WKY by a combination of subcutaneous implants of DOCA (between 100 and 200 mg of DOCA/kg body weight) mixed in Silastic and administration of 1% NaCl solution as drinking water. DS were fed standard rat food (Teklad, Madison, WI, USA; 20.8% protein) from 4 to 8 weeks of age. At 8 weeks of age, DS were fed a high salt diet (hypertensive group) or continued on a standard (normotensive control group) salt diet. High salt diets contained 7.2% NaCl and 0.7% KCl; normal salt diets contained 0.18% NaCl and 0.7% KCl. Some DS were started on high salt food at 10 or 12 weeks of age. The WKY were subdivided into two groups: 1) untreated WKY and 2) WKY undergoing sham production of renal hypertension. Because the sham operation did not affect the susceptibility of the blood-brain barrier to hypertensive disruption, the data for the normotensive WKY were grouped together.

Measurement and Duration of Chronic Hypertension

Blood pressure was monitored weekly in conscious rats using a tail plethysmographic technique (JITC, Woodland Hills, CA, USA). Disruption of the blood-brain barrier was studied after the rats had been hypertensive for at least 3 weeks. This criterion was chosen because previous studies have shown that vascular structural changes have occurred in the brain or other organs by that time. We defined hypertension in SHR, 2K1C rats, and DOCA-NaCl rats as a blood pressure measurement exceeding 150 mm Hg. Hypertension in DS fed a high salt diet was defined as a measurement greater than 15 mm Hg above the mean pressure in DS fed a low salt diet at the same age. Mean age was not different (p > 0.05) among the groups. Mean duration of hypertension was not different (p > 0.05) among the groups of hypertensive rats.

Hypertensive Disruption of the Blood-Brain Barrier

At the time of study, rats were anesthetized with sodium pentobarbital (50 mg/kg i.p.) and catheters were inserted in a femoral artery and vein to allow measurement of arterial pressure and for injection of drugs, respectively. Supplemental intravenous doses of pentobarbital were given if needed to maintain anesthesia. Bilateral superior cervical sympathectomy was performed to eliminate the effects of sympathetic nerves on cerebral vessels during seizure. The abdominal aorta near the diaphragm was exposed, and a length of silk suture was placed around the aorta and threaded through a piece of tubing. The rats were paralyzed by intravenous administration of gallamine (dose titrated to effect) and artificially ventilated.

We then injected 5 μCi of radioiodinated (125I) serum albumin (RISA; New England Nuclear, Boston, MA, USA) intravenously. Any changes in the pH of the blood were corrected by intravenous injection of a 7.5% solution of sodium bicarbonate. Three samples of arterial blood were taken 15, 25, and 35 minutes after the injection of albumin. Forty minutes after the injection of albumin, we injected bicuculline, 1.2 mg/kg, intravenously, which increases arterial pressure and breaks the blood-brain barrier. When blood pressure began to rise, the abdominal aorta was occluded. One more sample of arterial blood was obtained 45 minutes after the
injection of albumin. Ten minutes after the injection of bicuculline, saturated KCl was injected intravenously to kill the animal. The animals were then perfused transcardially with saline to flush out the albumin remaining in the blood vessels. Samples of the perfusate were obtained to confirm that most of the RISA was being removed by the perfusion. Disruption of the blood-brain barrier to RISA was measured in the forebrain, as described previously. Briefly, blood samples and sections of brain were placed in a gamma counter (Model 1150, Searle Analytic Laboratories, Des Plaines, IL, USA) for measurement of \( {^{125}}\text{I} \). The degree of disruption of the blood-brain barrier was measured as the ratio of \( {^{125}}\text{I} \) activity in the brain (divided by the weight of the tissue) divided by the amount of \( {^{125}}\text{I} \) activity in the blood sample (divided by the weight of the blood sample) taken 5 minutes after the injection of bicuculline. In addition, we calculated the clearance of the labeled albumin from the blood as described, to be sure that the results were not biased because of different clearances of albumin from the blood of the different groups of animals.

**Statistics**

Multiple comparisons of means were performed by ANOVA followed by Tukey's test for specific comparisons between individual means. If only two means were compared, Student's \( t \) test was used. Observations in SHR, 2K1C rats, and DOCA-NaCl rats were compared with those in WKY controls. Observations in DS fed a high salt diet were compared with those in DS fed a low salt diet using ANOVA. We also made comparisons between DS fed a low salt diet and WKY. The comparisons between DS fed standard rat chow and WKY were made using Tukey's test after an ANOVA performed on all six groups of rats. A probability level of less than 5% was considered significant for all statistical tests.

**Results**

Blood pressures of conscious rats are shown in Figure 1. The blood pressure taken in conscious rats just before the final study showed that SHR, 2K1C rats, DOCA-NaCl rats, and DS fed a high salt diet had significantly higher blood pressures than their normotensive controls. Blood pressure was not different \( (p > 0.05) \) among the hypertensive groups of rats (SHR, 2K1C rats, DOCA-NaCl rats, and DS fed high salt food). During the operation, the differences in blood pressure were not as great (Table 1), possibly due to the laparotomy that was performed to allow occlusion of the abdominal aorta.

Acute hypertensive disruption of the blood-brain barrier was less in SHR, DOCA-NaCl rats, and DS fed a high salt diet, but not in 2K1C rats, as compared with normotensive controls (Figure 2). Acute hypertensive disruption was greater in DS fed a low salt diet than in WKY (see Figure 2). Brain/blood RISA ratios were significantly less \( (p < 0.05) \) in control rats not subjected to acute hypertension (Figure 3) than in rats subjected to acute hypertension. The brain/blood RISA ratios did not differ between the groups of control rats not subjected to acute hypertension. Thus, the response to acute hypertension was not the result of different degrees of basal brain RISA transport between the groups of rats.

The increase in blood pressure during bicuculline administration combined with aortic occlusion is illustrated in Figure 4. The only significant difference in the change of blood pressure among groups was between 2K1C rats and WKY. To determine whether this difference in the degree of acute hypertension might account for the failure to observe the reduced blood-brain barrier disruption in 2K1C rats, we performed analysis of covariance on the disruption of the blood-brain barrier with the change of blood pressure (degree of acute hypertension) as a covariate. The results of that analysis showed that there was no difference in the disruption of the blood-brain barrier between 2K1C rats and WKY \( (p > 0.05) \). We also measured the rate of rise of blood pressure during acute hypertension, which was not different among the groups (see Table 1).

There were also some significant differences among groups for clearance of RISA from the blood and peak blood pressure reached during acute hypertension (see Table 1). In addition, there were some sizable differences (though not significant, \( p > 0.05 \)) in the amount of \( {^{125}}\text{I} \) activity remaining in the last sample of perfusate (see Table 1), which might have biased our results. However, analysis of covariance...
TABLE 1. Arterial Pressures and Disposition of 125I-Labeled Albumin in Rats Subjected to Acute Hypertension

<table>
<thead>
<tr>
<th>Group</th>
<th>Control (mm Hg)*</th>
<th>Peak (mm Hg)t</th>
<th>Rate of change (mm Hg/sec)t</th>
<th>Clearance of RISA (%)§</th>
<th>RISA remaining (%)fl</th>
<th>Duration of hypertension (wk)1</th>
</tr>
</thead>
<tbody>
<tr>
<td>DS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High salt diet</td>
<td>(n=8)</td>
<td>141±14</td>
<td>205±16</td>
<td>27±4</td>
<td>20±5.8**</td>
<td>2.8±1.3</td>
</tr>
<tr>
<td>Low salt diet</td>
<td>(n=10)</td>
<td>133±3</td>
<td>215±3</td>
<td>27±4</td>
<td>40±6.6</td>
<td>3.2±1.1</td>
</tr>
<tr>
<td>DOCA-NaCl rats</td>
<td>(n=7)</td>
<td>134±12</td>
<td>210±9</td>
<td>29±4</td>
<td>22±6.3</td>
<td>1.7±0.6</td>
</tr>
<tr>
<td>SHR</td>
<td>(n=10)</td>
<td>169±7**</td>
<td>237±6**</td>
<td>29±5</td>
<td>38±3.1</td>
<td>2.3±0.8</td>
</tr>
<tr>
<td>WKY</td>
<td>(n=10)</td>
<td>131±4</td>
<td>208±3</td>
<td>33±3</td>
<td>35±4.4</td>
<td>3.4±1.5</td>
</tr>
<tr>
<td>2K1C rats</td>
<td>(n=10)</td>
<td>154±5</td>
<td>252±5**</td>
<td>37±4</td>
<td>18±3.6**</td>
<td>2.6±1.3</td>
</tr>
</tbody>
</table>

Values are means ± 1 SEM. RISA = 125I-labeled albumin.

*Blood pressure after anesthetization and laparotomy.
†Highest mean arterial pressure after bicuculline plus aortic occlusion.
‡Change in blood pressure during acute hypertension divided by the time from just before the rise to the peak pressure.
§(RISA in blood 5 minutes before acute hypertension minus RISA in blood 5 minutes after acute hypertension)/(RISA in blood 5 minutes before acute hypertension).
fl(RISA in last sample of perfusate)/(RISA in first sample of perfusate).
*See Materials and Methods for a definition of the duration of hypertension.
**p < 0.05, compared with values in normotensive controls.

showed that these disparities did not explain the differences among groups with respect to hypertensive disruption of the blood-brain barrier.

We did not observe any difference among groups with respect to duration of hypertension (see Table 1), partial pressure of blood CO2 or O2, or pH (Table 2). Thus, these potentially confounding variables do not explain the differences in acute hypertensive disruption of the blood-brain barrier in the groups of rats.

Discussion

There are three major conclusions from this study. First, chronic hypertension reduces the susceptibility of the blood-brain barrier to acute hypertensive disruption. Second, 2K1C rats have an anomalous response to acute hypertensive disruption. Third, there may be a genetic influence on the susceptibility of the blood-brain barrier to acute hypertensive disruption.

The first conclusion is based on the observation that three of the four models of chronic hypertension showed reduced disruption of the blood-brain barrier during acute hypertension as compared with their normotensive controls. The reduced disruption of the barrier could not be attributed to the degree of acute hypertension, rate of change of blood pressure, blood gas and pH measurements, or disposition of RISA. In previous studies, the rate of change of blood pressure was not reported. The rate of change of blood pressure may be an important factor in hypertensive disruption of the barrier. Therefore, our study extends previous studies by showing that the rate of change of pressure does not explain the differences in the degree of acute hypertensive disruption of the blood-brain barrier. Thus,
However, the finding that three of four models of chronic hypertension do not reduce the disruption of the blood-brain barrier is not less than in controls. Our study extended earlier observations in that we measured the disruption of the blood-brain barrier at the same time as we measured it in the renal hypertensive rats. Thus, the experimental conditions were uniform across models, a situation not true of previous studies.

The observation that renal hypertensive rats do not show reduced disruption of the blood-brain barrier at acute hypertension suggests two hypotheses concerning the effect of chronic hypertension on acute hypertensive disruption of the blood-brain barrier. The first hypothesis is that there is no consistent effect of chronic hypertension on acute hypertensive disruption of the blood-brain barrier and that the results we have obtained are peculiar effects in each model. The second is that chronic hypertension usually reduces the susceptibility of the blood-brain barrier to acute hypertensive disruption, but that some unusual situation exists in renal hypertensive rats that results in no reduction of the susceptibility to acute hypertensive disruption of the blood-brain barrier. The results of our experiment do not decisively differentiate between these two possibilities. However, the finding that three of four models of hypertension behaved in a similar fashion favors the hypothesis that renal hypertensive rats have an unusual response as regards the protective effect of chronic hypertension on acute hypertensive disruption of the blood-brain barrier. Further experiments to differentiate between the two hypotheses will be necessary.

Our third important conclusion—that susceptibility to acute hypertensive disruption may have a genetic component—is a new finding, because no one else has measured disruption of the blood-brain barrier during acute hypertension in different strains of normotensive rats in the same experiment. Again, this effect was not secondary to differences in the degree of acute hypertension, rate of change of blood pressure, blood gas and pH measurements, or disposition of RISA. There are two hypotheses to explain the difference in susceptibility of the blood-brain barrier to acute hypertensive disruption between the two normotensive groups of rats.

The possibility that diet may have an important effect on the cerebral circulation deserves serious consideration, as diet affects the development of stroke in stroke-prone rats. However, this effect of diet on stroke is poorly understood. It has been reported that very high levels of dietary potassium protect against stroke. There are no data on how potassium affects acute hypertensive disruption of the blood-brain barrier. As our diets did not show a large difference in potassium content, differences in potassium content of the diet could not explain any of our results. It has also been reported that the diet that produces stroke in stroke-prone SHR is deficient in protein (19.7% in the Japanese diet vs 25.3% in the American diet). It has also been reported that a diet deficient in protein (but also high in salt) leads to an increase in the incidence of spontaneous opening of the blood-brain barrier in stroke-prone SHR. However, as this low protein and high salt diet also increased blood pressure, the effect of protein on the disruption of the blood-brain barrier is unclear. The importance of protein in the development of stroke was not noted in a preliminary report. In this study, a low protein diet did not affect blood pressure or the incidence of stroke. Thus, the effect of protein on cerebral circulation seems minimal. As our diets did not show a large difference in protein content, differences in the diet could not explain the difference in susceptibility of the blood-brain barrier to acute hypertensive disruption between the two normotensive groups of rats.

Table 2. Blood Gas Values and pH in Rats Subjected to Acute Hypertension

<table>
<thead>
<tr>
<th>Group</th>
<th>P02 (mm Hg)</th>
<th>PCO2 (mm Hg)</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>DS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High salt diet</td>
<td>(n=10)</td>
<td>130±6</td>
<td>37±0.6</td>
</tr>
<tr>
<td>Low salt diet</td>
<td>(n=10)</td>
<td>145±5</td>
<td>36±0.8</td>
</tr>
<tr>
<td>DOCA-NaCl rats</td>
<td>(n=7)</td>
<td>141±4</td>
<td>36±0.8</td>
</tr>
<tr>
<td>SHR</td>
<td>(n=10)</td>
<td>145±5</td>
<td>37±0.5</td>
</tr>
<tr>
<td>WKY</td>
<td>(n=10)</td>
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<td>37±0.6</td>
</tr>
<tr>
<td>2K1C rats</td>
<td>(n=10)</td>
<td>135±8</td>
<td>36±0.6</td>
</tr>
</tbody>
</table>

Values are means ± 1 SEM. P02 = partial pressure of O2; PCO2 = partial pressure of CO2.
difference in protein content, differences in the protein content of the diet could not explain any of our results.

The other possible explanation for the difference in the susceptibility of the blood-brain barrier to acute hypertensive disruption between normotensive rats is a consequence of some genetic difference between WKY and DS. Further experiments need to be done to determine which of the two hypotheses just outlined is correct.

Limitations of the Radiolabeled Albumin Technique

Some limitations of the technique used to assess disruption of the blood-brain barrier also need to be addressed. One limitation of the use of RISA to measure blood-brain barrier disruption is that this technique does not measure the permeability of the cerebral vasculature. Permeability is a measure of the transfer of substances across membranes measured per unit time and unit area available for transport. Although we controlled the amount of time between disruption of the barrier and the end of the experiment, we did not estimate the surface area available for transport of the labeled albumin molecules. Thus, our results could also possibly be explained by a reduced surface area of the vasculature available for transport in those groups showing reduced brain/blood ratios of RISA.

Another limitation of the technique is that it is not possible to know whether all intravascular RISA is removed at the end of the experiment. This is an important question, as differences in residual RISA between groups of animals would have an important effect on the brain/blood ratio of RISA. We attempted to estimate the clearance of RISA from the brain at the end of the experiment by measuring the amount of \(^{125}\text{I}\) activity left in samples of effluent during perfusion of the rats. We found that the final samples of effluent had very low concentrations of \(^{125}\text{I}\) (see Table 1). Also, if a significant fraction of RISA had been bound to blood vessels after perfusion, it would not have affected the conclusions that we have drawn unless differential binding of RISA occurred in the different groups of rats. We found that the brain/blood ratios of RISA were the same in the different groups of rats not subjected to acute hypertension (see Figure 3). This observation is consistent with the suggestion that there was no differential binding of RISA to the cerebral vessels among the groups of rats. Therefore, we believe that our results are not biased by the failure to clear residual RISA from the cerebral vascular space.

Mechanism of Acute Hypertensive Disruption of the Blood-Brain Barrier

To determine the mechanism of the differences in the susceptibility of the blood-brain barrier to acute hypertensive disruption, one must examine the mechanism of acute hypertensive disruption of the barrier. Until recently, acute hypertension was thought to disrupt the blood-brain barrier by changing the tension on the wall of arterioles, which somehow led to an increase in transendothelial transport of molecules across the arteriolar endothelium. Mayhan and Heistad have suggested that pressure changes in pial veins are important determinants of acute hypertensive disruption of the blood-brain barrier. They have observed that disruption of the blood-brain barrier begins in the veins and subsequently may occur in arteries. In addition, when they raised pial venous pressure to the same degree as that observed after arterial hypertension, they observed the same degree of disruption of the blood-brain barrier. Thus, the role of veins in acute hypertensive disruption of the blood-brain barrier seems to be important.

The role of changes in pial venous pressure in acute hypertensive disruption of the blood-brain barrier in rats with chronic hypertension has been examined. It has been reported that the increase in pial venous pressure during acute arterial hypertension is less in SHR than in WKY. When pial venous pressure was increased to the same extent in WKY and SHR, there was an equal degree of disruption in the two strains of rats. Thus, changes in pial venous pressure appear to explain the difference in susceptibility of the blood-brain barrier to acute hypertensive disruption between SHR and WKY. However, it is not known whether changes in pial venous pressure explain the differences among the other models of hypertension that we have studied. Specifically, it is not known whether pial venous pressure changes are similar in WKY and renal hypertensive rats, or if the change in pial venous pressure is less in WKY than in normotensive DS. Thus, experiments testing these hypotheses need to be done.

Experimental Stroke and Hypertensive Encephalopathy

The clinical implications of this work are not clearly defined. Hypertensive disruption of the blood-brain barrier may play a role in the development of stroke and hypertensive encephalopathy in hypertensive rats (though some disagree). The finding that most models of chronic hypertension show reduced susceptibility to acute hypertensive disruption of the blood-brain barrier would lead one to expect that stroke or hypertensive encephalopathy might not develop in those models of hypertension. However, stroke and hypertensive encephalopathy have been described in SHR (stroke-prone substrain), DOCA-NaCl rats, DS (fed high salt), as well as in renal hypertensive rats. Therefore, a reduced susceptibility of the blood-brain barrier to acute hypertensive disruption does not appear to be linked to a reduced propensity to have a stroke or hypertensive encephalopathy.

In summary, we found that chronic hypertension seems to protect the blood-brain barrier from acute hypertensive disruption, with the exception of renal hypertensive rats. These observations extend those
of previous studies. In addition, we found that the susceptibility of the blood-brain barrier to acute hypertensive disruption may differ among strains of normotensive rats. The susceptibility of the blood-brain barrier to acute hypertensive disruption did not seem to correspond to the tendency to have a stroke or hypertensive encephalopathy. The mechanism of these differences remains to be established.

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