Changes in Local Cerebral Blood Flow Following Bilateral Carotid Occlusion in Spontaneously Hypertensive and Normotensive Rats

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SUMMARY Local blood flow in the cortex and thalamus was measured by the hydrogen clearance method in spontaneously hypertensive rats (SHR) and normotensive rats (NTR) before and after bilateral carotid occlusion. There were no differences in the resting blood flow values between SHR and NTR. Following carotid occlusion cortical blood flow in SHR was markedly reduced to 17% of the resting level at 1 h and, further, to less than 10% at 3-5 h period, while in NTR it decreased only to 36-38% during 5 h occlusion. Thalamic blood flow in SHR was decreased to 39% at 1 hr and to below 20% at 3-5 h, while in NTR it remained approximately 40% of the resting level during 5 h occlusion. The blood flow reduction in either cortex or thalamus after carotid occlusion was much greater in SHR than in NTR. This difference was highly significant. The increased cerebral vascular resistance caused by persistent hypertension may play an important role in a greater reduction of blood flow in SHR after carotid occlusion. Relation of the blood flow reduction to the brain metabolism is discussed.

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PREVIOUS STUDIES have demonstrated that in comparison with normotensive rats (NTR), spontaneously hypertensive rats (SHR) have a greater increase in cerebral ischemic metabolites with a concomitant decrease in adenosine triphosphate following carotid occlusion, suggesting that SHR are more susceptible to cerebral ischemia. In SHR, an upward shift of cerebral blood flow autoregulation and a marked reduction of the cerebral perfusion pressure after carotid occlusion might be responsible for such susceptibility to cerebral ischemia.

To elucidate how bilateral carotid occlusion effects cerebral circulation, local cerebral blood flow in the cortex and thalamus was measured in SHR and NTR using the hydrogen clearance technique before and after carotid occlusion.

Methods

Seventeen male SHR and 15 male NTR, aged 5-9 months, were anesthetized with intraperitoneal amobarbital (10 mg/100 g body weight). Additional anesthesia was given as needed during the experiment. After tracheotomy, one femoral artery was cannulated for blood pressure recording with an electro-manometer and for anaerobic sampling for blood gas analysis.

Both common carotid arteries, exposed and separated carefully from the vagosympathetic trunks, were loosely encircled with sutures for later occlusion. The animal’s head was fixed in a head-holder, and a small burr hole was made in the skull 2 mm lateral to the bregma on each side. A Teflon-coated platinum electrode, 200 µm in diameter, with a 1 mm portion at its tip uncoated and plated with platinum black was placed in the cortex (2 mm in depth from the brain surface) and the another in the thalamus in the nucleus reticularis thalami (7 mm in depth) by using a stereotaxic apparatus. The reference electrode was an Ag-AgCl electrode inserted under the skin. Cerebral blood flow (CBF) was measured using a hydrogen clearance method by giving 10% hydrogen gas mixture under spontaneous breathing. The body temperature, as measured in the rectum, was kept close to 37°C.

After allowing more than 30 min for a steady state, at least 3 base-line CBF were measured at intervals of about 15 min and one arterial blood sample was obtained for gas analysis. Both carotid arteries were simultaneously occluded by pulling through the sutures which had previously been passed around the arteries. CBF was determined at 5 min and hourly up to 5 h after carotid occlusion. The second blood sample was obtained after 3-5 h of ischemia.

After termination of the experiment, each animal’s brain was grossly examined. When either an improper placement of the electrode or gross tissue damage by inserting the electrode was found, CBF data were excluded from the present results.

Results

Blood Pressure. Figure 1 shows the serial changes in mean arterial pressure (MAP) before and after carotid occlusion. In SHR, MAP rose to 123% of the resting level immediately after occlusion, followed by a gradual fall to 83% at 3 h and further to 75% at 5 h occlusion. In NTR, MAP increased to 121% after occlusion and stayed at the same level for the following 2 h, and thereafter, gradually returned to the resting level at 5 h occlusion.

Blood Gases. After carotid occlusion, arterial PCO₂ decreased from 38.8 to 26.6 mm Hg in SHR (p < 0.001) and from 39.1 to 33.8 mm Hg in NTR (p...
FIGURE 1. Changes in mean arterial pressure (MAP) before and after bilateral carotid occlusion in normotensive (NTR) and spontaneously hypertensive rats (SHR). An initial rise in MAP was followed by a fall below baseline 3 h after carotid occlusion in SHR. Bars represent ± SEM.

FIGURE 2. Changes in cortical blood flow before and after bilateral carotid occlusion in normotensive (NTR) and spontaneously hypertensive rats (SHR). Bars represent ± SEM.

FIGURE 3. Changes in thalamic blood flow before and after bilateral carotid occlusion in normotensive (NTR) and spontaneously hypertensive rats (SHR). Bars represent ± SEM.

TABLE Arterial Acid-base Parameters Before and After Carotid Occlusion in Normotensive (NTR) and Spontaneously Hypertensive Rats (SHR)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Carotid Occlusion (3-6 h)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 15</td>
<td>n = 10</td>
</tr>
<tr>
<td>Pco2 (mmHg)</td>
<td>39.1 ± 1.2</td>
<td>33.8 ± 2.3*</td>
</tr>
<tr>
<td>Pox (mmHg)</td>
<td>86.4 ± 6.0</td>
<td>93.7 ± 6.2</td>
</tr>
<tr>
<td>pH</td>
<td>7.415 ± 0.017</td>
<td>7.470 ± 0.028</td>
</tr>
<tr>
<td>SHR</td>
<td>n = 16</td>
<td>n = 11</td>
</tr>
<tr>
<td>Pco2 (mmHg)</td>
<td>38.8 ± 1.2</td>
<td>26.6 ± 2.9**</td>
</tr>
<tr>
<td>Pox (mmHg)</td>
<td>94.6 ± 5.4</td>
<td>100.7 ± 4.9</td>
</tr>
<tr>
<td>pH</td>
<td>7.414 ± 0.010</td>
<td>7.430 ± 0.019</td>
</tr>
</tbody>
</table>

Values are mean ± SEM, *p < 0.05, **p < 0.001.
human, and in our rats the CBF value was approximately one-half of that in awake rats. Cerebral autoregulation was well preserved and vasoreactivity to CO₂ was also satisfactory even in the anesthetized animals. Eklöf et al. have observed a 50% reduction of the frontoparietal cortical blood flow 30 min after bilateral carotid occlusion in male rats. Choki et al. found only a 34% reduction of the cortical blood flow 2 h after occlusion in female rats. Comparing these findings, the percent reduction of CBF was much greater in our NTR which had about 60% decrease in CBF at 4-5 hours after carotid occlusion. In the former 2 studies, the animals’ respiration was artificially controlled to maintain normocapnia during the experiment. Our animals, which were allowed to breathe spontaneously, tended to hyperventilate after carotid occlusion, probably due to a central neurogenic mechanism, and then became hypocapnic. Such hypocapnia appeared to be a main cause of an additional reduction of CBF in our NTR.

In SHR, CBF reduction following carotid occlusion was more pronounced and significantly different from that in NTR. An initial CBF decrease was followed by a further progressive reduction to less than 10% of the resting value in the cortex and below 20% in the thalamus at 5 h occlusion. In the thalamus blood is partly supplied from the vertebralbascular circulation. The progressive diminution of CBF seems due to secondary effects of ischemia-induced brain edema and also due to a gradual fall of systemic blood pressure. Such a great difference of CBF changes between SHR and NTR may be the result of a difference in the cerebral vascular resistance. The lower limit of cerebral autoregulation is shifted upwards in SHR (95 mm Hg of MAP) in contrast to NTR (62 mm Hg). Bilateral carotid occlusion leads to a greater decrease of the carotid back pressure in SHR (65 mm Hg or 74%) than in NTR (18 mm Hg or 26%). In consequence, carotid occlusion in SHR causes a pronounced reduction of perfusion pressure in the brain which is far below the lower limit of CBF autoregulation.

This study, together with previous metabolic studies, indicate there is a threshold of CBF (40% of the resting), below which normal brain metabolism is no longer maintained. Eklöf et al. have found that a CBF reduction to 45% of control is critical for keeping energy metabolism normal in the rat brain. Astrup et al. report that the ischemic threshold is approximately 15 ml/100 g/min or 35% of normal. Below this level electrical failures such as flattening of the EEG or ceasing of evoked cortical potential develop. When CBF is further lowered to about 6 ml/100 g/min, or 15% of normal, massive release of intracellular potassium ion and extracellular acidosis occurs. Ischemic metabolites in the rat brain increase 12 times and high energy phosphate significantly decreased in SHR 5 h after carotid occlusion. In SHR, cortical blood flow was found to be reduced to less than 10% of the resting value found in the present study, further, ischemic changes of the brain have been confirmed histologically and by electronmicroscopy.

The increased cerebral vascular resistance relevant to hypertension in SHR may play an important role in the significantly greater reduction of cortical and thalamic blood flow following bilateral carotid occlusion.

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References

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