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

MASATOSHI FUJISHIMA, M.D., TAKAO ISHITSUKA, M.D., YASUO NAKATOMI, M.D., KINYA TAMAKI, M.D., AND TERUO OMAE, M.D.

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.

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 electromanometer 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
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 ± 1 SEM.

Blood Flow. Average values for cortical CBF in the resting state were 41.6 ± 2.7 (SEM) ml/100 g/min in SHR and 39.4 ± 3.0 ml/100 g/min in NTR, this difference was not significant. Within 5 min after occlusion CBF in SHR decreased markedly to 13.1 ± 1.7 ml/100 g/min or 31% of the resting, and further to 7.1 ± 1.4 ml/100 g/min or 17% at 1 h of ischemia (fig. 2). During 2–5 hours of occlusion, CBF remained extremely low at 3.6–3.9 ml/100 g/min or approximately 9% of the resting value. Cortical CBF in NTR was decreased less, and remained 36–38% of the resting level throughout 5 h of occlusion. There were pronounced differences in the cortical blood flow reduction after carotid occlusion between SHR and NTR (p < 0.001).

Thalamic CBF averaged 49.2 ± 4.0 ml/100 g/min in SHR and 47.1 ± 3.7 ml/100 g/min in NTR. This difference was not significant. Immediately after carotid occlusion, thalamic CBF in SHR decreased markedly to 19.2 ± 2.2 ml/100 g/min or 39% of the resting value, followed by a further reduction to 8.3 ± 1.7 ml/100 g/min or 16.8% at 5 h occlusion (fig. 3). The CBF reduction in the thalamus was less marked than that in the cortex. Thalamic CBF in NTR was reduced to 22.4 ± 1.7 ml/100 g/min or 48% immediately after occlusion and remained at a constant level during 2–5 hours occlusion. The reduction of thalamic CBF in NTR was significantly smaller than that in SHR, but almost the same as that of cortical CBF in NTR.

Discussion

The hydrogen clearance technique has been widely used for the measurement of CBF in a variety of laboratory animals. CBF values obtained by using this method are compatible with those measured by \(^{133}\)Xe clearance technique, a radioautographic method and a microsphere technique.

It has been noted that deep barbiturate anesthesia causes a 50% reduction of CBF in animals and...
In SHR, cerebral 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.

Acknowledgment

The authors thank Miss Yamaguchi for preparing this manuscript.

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doi: 10.1161/01.STR.12.6.874

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