where the concentration in the albumin Ringer is low, quantification was performed by comparing the X-ray peaks of the tissue with that of the Cl peak in the albumin layer, taking into account the experimentally determined differences in the X-ray yield for equal concentrations of the elements. The Figure presents 5 typical X-ray spectra together with a schematic view of a nerve fibre section with a node of Ranvier. The capitals indicate the different locations of the scanned areas on which the analysis was performed. The Table gives the corresponding count rates for the characteristic X-rays and the continuous radiation. The spectrum obtained from the albumin layer (A) shows high Na and Cl but low K and P peaks, corresponding to a typical extracellular pattern. A similar spectrum is obtained in the interstitial space of the nerve (B). In contrast, the spectrum obtained in the axon of a nerve fiber (C) shows small peaks for Na and Cl, but a large K peak. Compared to cellular spectra from other tissues[4], the P peak is relatively small. The wet weight concentrations (mmol/kg wet wt.) computed using the albumin layer as a standard are Na = 90, P = 2, Cl = 84, K = 4 for the interstitial space, and Na = 17, P = 17, Cl = 10, K = 81 for the axon. The values obtained for the axon are in agreement with those determined by other methods[5]. The spectra obtained from the myelin sheath of the nerve fibre (D, E) are characterized by high peaks of P, Cl and Na and a low K peak. As indicated by the high background radiation, the mass content of this structure exceeds several fold that of the albumin. Since the relation between the respective intensities of the characteristic X-rays obtained from samples with large differences in mass content is not known, a comparison of the myelin X-ray spectra with the albumin spectrum cannot provide reliable quantitative data for the element-distribution within the myelin sheath. Nevertheless it is obvious from the Figure that the spectra from these structures show an extracellular pattern with high Na, Cl and low K peaks. The very high P peaks are consistent with the high content of phospholipids in the myelin sheath[6]. It It should be noted that the myelin sheath close to the node of Ranvier exhibits higher peaks for Na and Cl than the internodal one as seen in the Figure (D, E). This observation seems to be a real effect and cannot be accounted for by differences in the mass content in the excited volumes, since the background radiation in both spectra (D, E) is of similar size.

The presence of a high Na concentration in the myelin sheat, particularly in the paranodal part of this structure is consistent with the 'synapse hypothesis' which assumes a Na storage in the paranodal region of the node of Ranvier. However, these measurements do not provide any information about the state of Na present in the myelin sheath, whether it is bound or exchangeable. Therefore, the functional significance of this Na remains uncertain.

Count rates of the K-α radiation of Na, P, Cl and K and the 'Bremsstrahlung' obtained on different structures of a freeze dried frog nerve section.

	Na	P	Cl	K	'Bremsstrahlung'
	(counts/sec)				
A) albumin layer	38.6	3.5	140.2	9.0	198
B) interstitial space	25.7	2.2	112.0	6.3	150
C) axonal space	5.2	20.6	14.2	125.9	127
D) myelin, internodal	33.5	334.8	82.5	35.2	1142
E) myelin, close to node	61.6	314.4	234.5	50.0	1275

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Lower Limit of Cerebral Autoregulation in Normotensive and Spontaneously Hypertensive Rats

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Summary. Cerebral autoregulation was examined in NTR and SHR. The lower blood pressure limit of autoregulation being 95 mm Hg in SHR was shifted upwards from 62 mm Hg in NTR.

Cerebral blood flow is kept constant despite a wide range of cerebral perfusion pressure in normal humans as well as animals under normocapnia, whereas the lower limit of autoregulation (the pressure below which cerebral blood flow decreases) varies depending on the habitual blood pressure level[1]. In the present study, we tested the cerebral autoregulation in normotensive and spontaneously hypertensive rats to find whether or not the lower limit of autoregulation is shifted upwards in hypertensive rats.

Methods. 6 normotensive rats (NTR) and 11 spontaneously hypertensive rats (SHR), weighing from 350 to 400 g, were anesthetized with i.p. amobarbital of 10 mg per 100 g of body weight. Tracheotomy was performed, and their respiration was controlled mechanically. One femoral artery was cannulated for blood pressure recording with an electromanometer and for blood sampling. After a midline incision of scalp, a small hollow screw was introduced into 2 mm anterior of the confluence sinus through a 2 mm burr hole allowing cerebral venous blood sampling. After completing the operation, a resting period of 30 min was allowed before the experiment. $^1/_2$ ml of each arterial and cerebral venous blood was withdrawn anaerobically for gas analysis by IL meter of Model 113.

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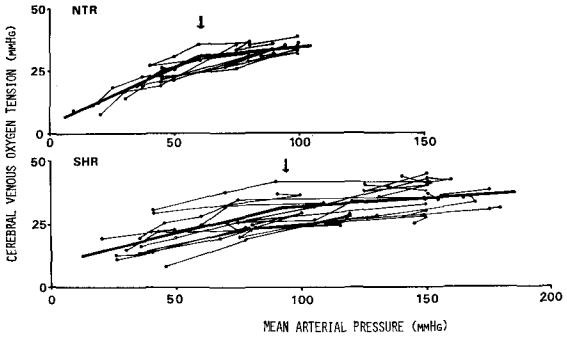
Cerebral venous oxygen tension ($cPvO_2$), corrected by a standard pH, was used as an index of cerebral blood flow.

Arterial carbon dioxide tension ($PaCO_2$) was maintained ranging between 33 and 43 mm Hg at the control state, and then systemic blood pressure was lowered stepwise by bleeding animals or by i.p. injection of hypotensive agents such as hexamethonium or phentolamine. After reaching the different blood pressure level and remaining for at least 5 min constant, another blood sample was obtained. At the hypotensive state below 40 mm Hg of mean arterial pressure (MAP) in NTR or 60 mm Hg in SHR, the respiration rate was reduced arbitrarily for preventing the lowering of $PaCO_2$.



Cerebral autoregulation in normotensive and spontaneously hypertensive rats. Cerebral venous oxygen tension is an index of cerebral blood flow. The lower blood pressure limit of cerebral autoregulation (arrow mark) is 62 mm Hg in NTR and 95 mm Hg in SHR, respectively.

Table I. Correlation of mean arterial pressure (MAP) to cerebral venous oxygen tension ($cPvO_2$) in NTR and SHR

Group	MAP range (mm Hg)	Regression equation	Correlation coefficient (r)	Probability (p)
NTR	60–100	$y = 0.08x + 25.9$	0.315	> 0.10
	< 60	$y = 0.45x + 4.07$	0.886	< 0.001
SHR	90–180	$y = 0.06x + 26.1$	0.234	> 0.10
	< 90	$y = 0.23x + 9.67$	0.620	< 0.001

y, $cPvO_2$ (mm Hg); x, MAP (mm Hg).

Table II. Arterial carbon dioxide tension ($PaCO_2$) at various MAP level in NTR and SHR

Group	MAP range (mm Hg)	No. of determination	$PaCO_2$ (mm Hg)
NTR	≥ 80	9	36.9 ± 1.2
	60– 79	7	37.7 ± 1.6
	40– 59	7	36.0 ± 1.6
	< 40	8	26.6 ± 1.5
SHR	≥ 140	10	35.4 ± 1.2
	100–139	8	38.0 ± 1.9
	60– 99	9	33.0 ± 2.2
	< 60	11	28.1 ± 2.0

Values are mean $\pm$ SEM.

When the experiment was completed, the brain and the skull with a screw removed en bloc for gross observations of venous cannulation and surface of the brain. The animals were discarded if their brain was damaged by the placement of a hollow screw.

Results. The Figure depicts the relationship between MAP and $cPvO_2$ as cerebral blood flow indicator in NTR and SHR. The lower blood pressure limit of autoregulation was 62 mm Hg in NTR and 95 mm Hg in SHR. At MAP ranging from 100 to 60 mm Hg in NTR, $cPvO_2$ remained unchanged despite changes in MAP, indicating that cerebral autoregulation was normally functioning, whereas at MAP below 60 mm Hg there was a highly significant correlation between 2 parameters as shown in Table I ($r = 0.886$, $p < 0.001$), indicating the impairment of autoregulation. In SHR, cerebral autoregulation was preserved normally at MAP ranging from 180 to 90 mm Hg, below which $cPvO_2$ was decreased as MAP fell, correlation between 2 parameters being highly significant ($r = 0.620$, $p < 0.001$). Cerebral PvO_2 at the autoregulatory range of MAP being 35 mm Hg was the same in both NTR and SHR.

Table II summarizes $PaCO_2$ in NTR and SHR at the various MAP level. $PaCO_2$ remained unchanged during MAP range from 100 to 40 mm Hg in NTR, and from 180 to 60 mm Hg in SHR, respectively, below which level $PaCO_2$ was apparently lowered despite the respiration being controlled mechanically by reducing the rate. Cerebral PvO_2 had already decreased below the resting value at the low pressure level before $PaCO_2$ started to fall. Therefore, a concomitant hypocapnia at severe hypotension may not have a direct influence on the level of the lower limit of cerebral autoregulation in either group.

Discussion. A linear correlation was found to exist among the internal jugular PvO_2, cerebral blood flow and $PaCO_2$ in healthy subjects[2,3]. It indicates that $cPvO_2$ might provide a useful index of cerebral blood flow. In the present study, $cPvO_2$ with correction by a standard pH was employed as an indicator of cerebral blood flow, since this correction might minimize the variation of $cPvO_2$ due to an individual difference in pH or PCO_2, and represent the more accurate value of cerebral blood flow.

Many observations indicate that the lower limit of cerebral autoregulation lies between 50 and 80 mm Hg of MAP in normal subjects as well as in animals[4–7], whereas in hypertensive patients it is shifted to the higher blood pressure level[1]. Possibly this is a mechanical effect as a consequence of hypertrophy of the arteriolar walls.

Either carotid or vertebral system is well developed in NTR as well as SHR. The configurations of the circle of Willis do not differ in both groups. Though statistically insignificant, the diameter of major cerebral arteries, posterior communicating artery and basilar artery is somewhat smaller in SHR than in NTR[8]. However, there is neither thickening of the vessel walls nor abnormalities of the ultrastructure of intracerebral and pail arteries in both groups[8].

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Although the morphological difference of the cerebral vasculature between NTR and SHR is minimal, vasodilatory response of cerebral arteries to the lowering of MAP seems insufficient in SHR, resulting in the lower limit of autoregulation to be shifted to 95 mm Hg of MAP, which is apparently higher than that in NTR.

The lower limit of autoregulation is also altered by anesthetic or changes in $PaCO_2$[9,10]. Hypercapnia may totally impair the autoregulation or raise the lower limit upwards, whereas hypocapnia may have an adverse effect on the autoregulation.

In our previous studies, bilateral carotid artery occlusion caused an extremely high mortality[11], a marked increase in anaerobic glycolytic metabolites of the brain[12], and diffuse-extensive cerebral infarcts in SHR[8], while a lower mortality, a minimal increase in metabolites and small-circumcribed infarcts were observed in NTR. These biochemical and histological changes following bilateral carotid occlusion in SHR seem attributed to the hemodynamic difference rather than the morphological difference of the cerebral arteries between two groups. It is likely that cerebral perfusion pressure following carotid occlusion might fall below the lower limit of autoregulation in SHR, but not in NTR.

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Carotid Back Pressure Following Bilateral Carotid Occlusion in Normotensive and Spontaneously Hypertensive Rats

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Summary. In SHR, CBP fell markedly and remained below 50 mm Hg after carotid occlusion despite SBP being elevated, while in NTR changes in CBP were related with changes in SBP. Vascular resistance of the brain in hypertensive rats is discussed.

Bilateral carotid artery occlusion causes a diffuse and extensive cerebral infarction in spontaneously hypertensive rats (SHR)[1], resulting in a great increase in lactate and lactate-pyruvate ratio[2], and a high mortality[3], whereas in normotensive rats (NTR) it causes a minimal metabolic and histological change of the brain. These observations suggest that cerebral perfusion pressure following bilateral carotid occlusion might fall by a greater extent beyond the lower limit of cerebral autoregulation in SHR than in NTR, with consequently severe ischemic changes of the brain. In the present study, carotid back pressure as an index of cerebral perfusion pressure was measured before and after carotid occlusion in NTR and SHR.

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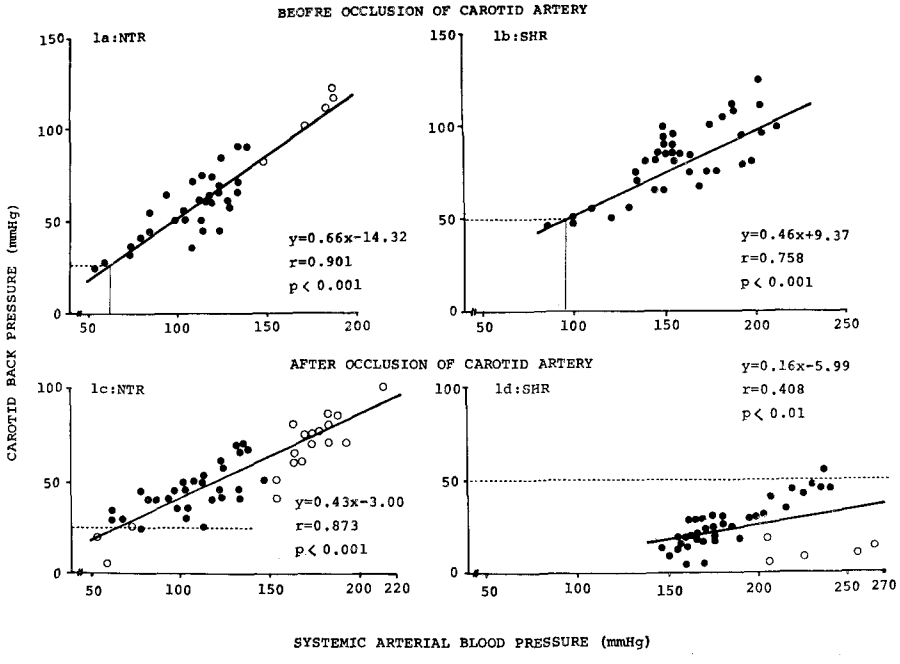

Fig. 1. Correlation between carotid back pressure and systemic blood pressure before and after bilateral carotid artery occlusion in normotensive rats (NTR) and spontaneously hypertensive rats (SHR). Open circle indicates systemic blood pressure being changed by drugs or bleeding. A dotted line designates a critical carotid back pressure level calculated from the lower systemic blood pressure limit of cerebral autoregulation (a solid line).