Hemodynamic Responses of the Venous System during Global Brain Ischemia Related to the Reflex Bradycardia in the Rabbit

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Abstract Global brain ischemia in anesthetized rabbits induces a pressor response, bradycardia, apnea, and a reduction in cardiac output. The bradycardia is virtually abolished by bilateral aortic denervation (ADN). To elucidate hemodynamic responses in the venous system and the role of bradycardia in these responses during brain ischemia, central venous pressure (CVP), femoral venous pressure (FVP), and circulation time (CT) of a dye in large veins were simultaneously measured before and after ADN. Cardiopulmonary blood volume (CPBV) and circulating blood volume (CBV) were also measured using a dye-dilution technique in separate experiments. Before brain ischemia, the value of CVP, FVP, mean arterial pressure (MAP), and heart rate (HR) were 0.2 ± 1.2 cmH$_2$O, 8.9 ± 1.9 cmH$_2$O, 76 ± 16 mmHg, and 274 ± 35 beats/min, respectively (n = 8, mean ± SD). During brain ischemia, CVP, FVP, and MAP significantly increased to 5.8 ± 2.6 cmH$_2$O, 11.1 ± 2.4 cmH$_2$O, and 159 ± 10 mmHg, respectively. HR decreased to 113 ± 54 beats/min. After ADN, the changes of CVP, FVP, and HR evoked by brain ischemia were significantly suppressed to 2.4 ± 1.6 cmH$_2$O, 9.8 ± 2.1 cmH$_2$O, and 210 ± 61 beats/min, respectively; however, the increase in MAP was not affected. During brain ischemia, CVP correlated negatively with HR, and positively with CT. CPBV tended to decrease and CBV significantly increased by 3.7 ± 2.5 ml/kg from that before brain ischemia. It seems that the increased amount in CBV evoked by brain ischemia mainly exists in large veins. From these results we conclude that bradycardia is a major determinant of the blood volume in the cardiopulmonary system and prevents its overflow into pulmonary circulation during global brain ischemia in the rabbit when afterload to the left ventricle is extremely increased.

Key words: global brain ischemia, venous system, bradycardia, blood volume, venous pressure.

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The global brain ischemia, which is produced by bilateral occlusion of the common carotid and vertebral arteries [1] in anesthetized rabbits, causes characteristic effects, such as a pressor response [1, 2], reduction in cardiac output [3], reflex bradycardia [4, 5], apnea [1, 6], and convulsion [1]. The bradycardia evoked by brain ischemia is mainly mediated through the afferent inputs from aortic baroreceptors because bradycardia during brain ischemia is virtually suppressed by bilateral aortic denervation [4, 5]. In some rabbits, gasping-like respiration occurs when the occlusion of the four vessels is sustained for over approximately 60 s [6].

Similar patterns of bradycardia are observed during intracranial hypertension [7–9] and diving [10]. The physiological meaning of bradycardia in these conditions is an important subject. Shimizu and Miyakawa [3] suggested that the role of bradycardia observed during brain ischemia is to maintain the efficiency of the mechanical work in the heart. However, the bradycardia does not affect pressor response and the decrease in ascending aortic flow evoked by brain ischemia [2, 5]. We recently reported that circulation times in the large arteries and veins are prolonged during brain ischemia, and there is a significant linear relationship between heart rate and the inverse of circulation time in the large veins, but not in the large arteries [11]. These facts have led us to come to the question whether the bradycardia can affect the hemodynamic changes in the venous system or not. Although circulatory responses of the arterial side to the global brain ischemia in the rabbit have extensively studied [2–5, 11], the hemodynamic changes of the venous system during brain ischemia have not been analyzed in detail. Only Takeuchi et al. showed that neurogenic constriction in the portal [12], mesenteric and femoral veins [13] is evoked by graded brain ischemia.

The aims of this study are to elucidate the hemodynamic changes in the large veins during brain ischemia and how it is related with brain ischemia-induced bradycardia.

**METHODS**

**Preparation.** A total of twenty-two rabbits of both sexes, weighing 2.8 ± 0.5 kg (mean ± SD), were anesthetized with urethane (1 g/kg, i.p.) and additional doses of this anesthetic agent (0.25 g/kg) were administered as needed. The trachea was incised and cannulated to allow spontaneous breathing with room air. The animal was fixed supine on a thermostatically regulated operating table and the body temperature was maintained at around 37°C.

The procedure to produce brain ischemia has been described in detail elsewhere [1, 3, 5]. In brief, the vertebral arteries were irreversibly occluded at the level of the third and/or fourth vertebrae. Then the common carotid arteries were reversibly occluded by clamps for approximately 30 s. A nearly complete interruption of the brain blood flow was further confirmed by the presence of apnea [1].

**Measurements of hemodynamic parameters.** Central venous pressure (CVP) was measured using a pressure transducer through a catheter inserted into the right
atrium via the right jugular vein. Femoral venous pressure (FVP) was measured also using a pressure transducer through a catheter, the tip of which was placed in the right femoral vein and oriented toward the heart. Each venous pressure was electrically averaged with time constant of 3s. The “physiologic reference point” [14] for measuring venous pressure was selected at the height which was 60% of the chest thickness from the back. After the experiments, the height of the tip of the catheter from the reference point was measured to estimate the true value of venous pressure. Then pressure gradient (PG) in large veins was calculated according to the following formula: PG = FVP - CVP - [hydrostatic pressure difference between the tips of two catheters for measurement of CVP and FVP].

Circulation time (CT) in large veins, cardiopulmonary blood volume (CPBV) and circulating blood volume (CBV) were measured using a dye-dilution technique. To measure CT, two catheters were used in the following procedures: one was placed in the left femoral vein for bolus injection of the dye (indocyanine green, 0.3 mg in 0.3 ml saline solution, Daiichi Seiyaku), and the other was placed in the right atrium for blood sampling into the cuvette (DYE MAC EW-90, ERMA, Fig. 1). The rate of suction was 0.067 ml/s. The latency of appearance time between the tip of the catheter and the cuvette was measured in a separate experiment, and appearance time and peak concentration time were corrected by

![Diagram](image)

**Fig. 1.** Measurement of central venous pressure, femoral venous pressure and circulation time. rt, right; ext, external.

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subtracting the latency from the values of CTs obtained through the dye-dilution curves. Suction of blood to obtain dye-dilution curve during brain ischemia was started at the time of the onset of brain ischemia. Dye was injected when the blood pressure curve reached a plateau.

To measure CPBV, that is the sum of intrapulmonary-vascular blood volume and intracardiac blood volume, the dye (indocyanine green, 0.3 mg in 0.3 ml saline solution) was bolusly injected through a catheter placed in the venous ostium of the right atrium. The blood was sampled into the cuvette through a catheter placed in the root of the ascending aorta. Cardiac output (CO) and mean transit time (MTT) were measured using the Stewart-Hamilton method [15]. CPBV was calculated as follows [16]:

$$\text{CPBV (ml/kg)} = (\text{CO}/60) \times \text{MTT/BW},$$

Where CO (ml/min), cardiac output; MTT (s), mean transit time of the dye; BW (kg), body weight of the animal.

To obtain the values of CO and MTT, the heights of the dye-dilution curves (Fig. 2) were manually measured every 0.5 s and reconstructed on a semi-logarithm graph paper. The linear portion of the down slope of this curve was extrapolated to zero and the area of the first circulation of dye was determined. In this series of experiments, we found that the reduction in O₂ saturation of hemoglobin due to apnea lineally elevated the baseline of dye-dilution curve as a function of time, because the elevation of the baseline was abolished by an artificial ventilation applied to the rabbit during apnea, and that the occurrence of gasping provoked by brain ischemia caused fluctuation of the baseline. Thus, we selected the rabbits

A

B

10 sec

Respiratory Movement

Arterial Pressure

Mean Arterial Pressure

Heart Rate

Dye-dilution Curve

Fig. 2. An example of typical records of respiratory movement, arterial pressure, heart rate, and dye-dilution curve, when cardiac output and mean transit time were measured before (A) and during (B) brain ischemia. Arrows on the dye-dilution curves show the time when the dye was injected.

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which did not show any gasping-like respiration during brain ischemia, and calculated the values of CO and MTT by measuring the height of the curve from the elevated baseline on the dye-dilution curves (Fig. 2B). MTT was corrected by subtracting the delay time from the values obtained from the dye-dilution curves.

To measure CBV, Evans blue (2 mg in 1 ml saline solution) was injected into the right femoral vein, and the blood (approximately 1 ml) was sampled twice from the left femoral artery. After first blood sampling was taken to obtain a control value at 9 min after dye injection, the brain ischemia was produced. When the pressor response became the maximum at 29±9 s after the onset of brain ischemia, the blood was again sampled for measuring CBV during brain ischemia. CBV was calculated as follows:

\[
\text{CBV (ml/kg)} = 100 \times I / \{C(100 - Ht)\} / \text{BW},
\]

where \( I \) (mg), dose of injected dye; \( C \) (mg/ml), plasma concentration of dye; \( Ht \) (%), hematocrit; \( \text{BW} \) (kg), body weight of the animal.

Arterial pressure was measured with a pressure transducer through a catheter inserted into the right femoral artery. The pulse pressure was electrically averaged with time constant of 3 s to record the mean arterial pressure (MAP). Heart rate (HR) was counted from pulse waves using a cardiotachometer. Respiratory movement (RM) was recorded by connecting the tracheal tube to a pneumotachometer. Heparin (1,000 unit/kg) was administered into the right atrium through a catheter inserted via the right external jugular vein.

Protocol. Experiments were divided into three groups. In the first group, the responses of CVP, FVP, and CT to brain ischemia were observed and the pressure gradient between two points for measuring CVP and FVP was calculated for both before and after bilateral aortic denervation in 8 rabbits. In the second group, CPBV was measured before and during brain ischemia in 7 rabbits which showed no gasping-like respiration. In the last group, CBV was measured before and during brain ischemia in 7 rabbits.

Statistics. An average of the data was expressed as mean±standard deviation (SD). For statistical evaluation, a regression line was obtained by the least square method. The difference between before and during brain ischemia in CPBV and CBV were tested by using a paired \( t \)-test. A two-way analysis of variance (ANOVA) was used to test the effect of brain ischemia and aortic denervation on CTs, the time course changes in CVP, FVP, PG, and a difference in each pressure. When the significant difference was obtained by ANOVA, a modified \( t \)-test was used for comparisons between the data obtained under the two different situations [17]. A probability value (\( p \)) less than 0.05 was considered significant.

Care of the animals. Care and experiments on all animals used in the present study were carried out according to the Guiding Principles for the Care and Use of Animals in the Field of Physiological Sciences approved by the Council of the Physiological Society of Japan as well as the Guidelines on Animal Experiments in Fukushima Medical College.

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RESULTS

Changes of venous pressures during brain ischemia and the effect of bilateral aortic denervation on these changes

Figure 3 shows the responses of central venous pressure (CVP), femoral venous pressure (FVP), and dye-dilution curve evoked by brain ischemia before (Fig. 3A) and after (Fig. 3B) bilateral aortic denervation in a rabbit. Before aortic denervation, the brain ischemia produced increases of CVP and FVP, prolongation of circulation time (CT), and a marked bradycardia accompanied with hypertension and apnea. After aortic denervation, the increases in CVP and FVP, prolongation of CT, and the bradycardia evoked by brain ischemia were largely suppressed although hypertension and apnea were not affected.

Figure 4 shows the summarized results of the changes in venous pressures, mean arterial pressure (MAP) and heart rate (HR). Before aortic denervation, the brain ischemia raised CVP and FVP to 5.8 ± 2.6 (the maximum value: 10.4, minimum value: 1.0) cmH$_2$O and 11.1 ± 2.4 (14.7–7.8) cmH$_2$O, respectively, at 30 s after the onset of brain ischemia, from 0.2 ± 1.2 (1.8 to −2.4) and 8.9 ± 1.9 (12.3–6.6) cmH$_2$O, observed before brain ischemia respectively (Fig. 4A, B, solid line). The amount of increase in CVP and FVP estimated at 30 s from the values obtained before brain ischemia were 5.6 ± 2.3 and 2.2 ± 1.0 cmH$_2$O, respectively. The former was significantly larger than that of the latter. Pressure gradient (PG) during brain

![Diagram](image-url)

**Fig. 3.** An example of responses of central venous pressure, femoral venous pressure, and dye-dilution curve in large veins to brain ischemia with records of respiratory movement, arterial pressure, and heart rate before (A) and after (B) bilateral aortic denervation. Arrows on the dye-dilution curves show the time when the dye was injected.
ischemia in rabbits with intact aortic nerves decreased to 2.3±1.7 cmH₂O at 30s from 5.7±2.6 cmH₂O before brain ischemia (Fig. 4C, solid line).

After aortic denervation, CVP and FVP measured before brain ischemia were −0.1±1.4 and 9.1±2.3 cmH₂O, respectively. These values were not significantly different from those in the rabbits with intact aortic nerves. CVP and FVP increased to 2.4±1.6 and 9.8±2.1 cmH₂O, respectively, at 30s during brain ischemia; however, the amount of increase in both pressures were significantly smaller as compared with that shown before aortic denervation (Fig. 4A, B, broken lines). After aortic denervation, PG was 6.1±2.7 cmH₂O before brain ischemia, and this value was not significantly different from that in the rabbit with intact aortic nerves. During brain ischemia; however, PG decreased only to 4.4±2.6

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**Fig. 4.** Changes in venous pressures, mean arterial pressure, and heart rate during brain ischemia and effects of bilateral aortic denervation on these changes. A: Central venous pressure. B: Femoral venous pressure. C: Pressure gradient between the points for measuring central and femoral pressure. D: Mean arterial pressure. E: Heart rate. Solid lines show the changes with intact aortic nerves and broken lines show the changes after aortic denervation. P: the values when the flow of the both common carotid arteries was maintained. L: steady state values after only the left common carotid artery was occluded. Numbers under the horizontal line show the time after occluding the right common carotid artery (0s). Values are mean±SD. *(p<0.05) and **(p<0.01) are significantly different from the values with intact aortic nerves.
cmH$_2$O from the value before brain ischemia (Fig. 4C, broken line), and the decrease was significantly smaller than that evaluated before the denervation.

At 30 s after the onset of brain ischemia before aortic denervation, MAP increased to 159±10 mmHg from 76±16 mmHg of the control before brain ischemia, and HR decreased to 113±54 beats/min from 274±35 beats/min before brain ischemia (Fig. 4D, E, solid line). After aortic denervation, the value of MAP and HR before brain ischemia was 78±18 mmHg and 281±29 beats/min. During brain ischemia MAP increased to 165±13 mmHg and HR decreased to 210±61 beats/min at 30 s. The increase in MAP was not significantly affected by aortic denervation, however, the reduction in HR was significantly suppressed by aortic denervation (Fig. 4D, E, broken line).

CVP and PG showed a significant correlation with HR (Fig. 5), but FVP did

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Fig. 5. Relationship between heart rate and venous pressure during brain ischemia.  
A: Heart rate and central venous pressure.  B: Heart rate and pressure gradient.

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not, when the data during brain ischemia before and after aortic denervation were plotted on the same graph.

Changes of circulation time during brain ischemia and the effect of bilateral aortic denervation on these changes

During brain ischemia before aortic denervation, the appearance time and peak concentration time of dye in the large veins were prolonged (Table 1). After the denervation, the prolongation of the appearance and peak concentration time were significantly suppressed.

Appearance time and peak concentration time significantly correlated with CVP (Fig. 6A), and the prolongation of CTs also significantly correlated with the decrease in pressure gradient (Fig. 6B) when the data during brain ischemia before and after the denervation were plotted on the same graph.

Changes of cardiopulmonary and circulating blood volume during brain ischemia

In all 7 animals tested for measurements of cardiopulmonary blood volume

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<tr>
<th>Table 1. The effects of bilateral aortic denervation (ADN) on circulation times in large veins.</th>
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<td>After ADN</td>
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Values are mean±SD in 8 rabbits. ADN, after bilateral aortic denervation; APT, appearance time; PT, peak concentration time. **(p<0.01) is significantly different from the value before brain ischemia with intact aortic nerves. ##(p<0.01) is significantly different from the value during brain ischemia with intact aortic nerves.

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<th>Table 2. Changes of cardiopulmonary blood volume and other hemodynamic parameters during brain ischemia.</th>
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<td>CPBV (ml/kg)</td>
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<td>HR (beats/min)</td>
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Values are mean±SD in 7 rabbits. CPBV, cardiopulmonary blood volume; MTT, mean transit time; CO, cardiac output; MAP, mean arterial pressure; HR, heart rate. **(p<0.01) is significantly different from the value before brain ischemia.
(CPBV), mean transit time (MTT) was prolonged and cardiac output (CO) was reduced during brain ischemia as compared with these values before the ischemia (Table 2). CPBV decreased in 6 animals, but in one animal, it increased to 10.1 ml/kg from 8.3 ml/kg. The bradycardia in 5 of 6 rabbits which showed the decrease in CPBV were less than 200 beats/min. The average CPBV in the 5 rabbits before and during brain ischemia were 9.4±3.4 and 8.6±3.4 ml/kg, respectively.

During brain ischemia CBV increased significantly to 66.6±12.2 ml/kg at 29±9s after the onset of brain ischemia from 62.9±10.0 ml/kg detected before brain ischemia.

Fig. 6. Relationship between venous pressures and circulation times during brain ischemia. A: Central venous pressure and circulation times. B: Decrease of pressure gradient and prolongation of circulation times. +, appearance time; △, peak concentration time.
DISCUSSION

Major findings from this study on hemodynamics in the venous system during brain ischemia are as follows: central and femoral venous pressures were elevated and circulation time was prolonged; and these changes were suppressed by bilateral aortic denervation which eliminated the brain ischemia-induced bradycardia without any changes in the pressor responses. Circulating blood volume increased, but cardiopulmonary blood volume decreased except in one case in which no bradycardia appeared during brain ischemia. We will discuss the meaning of the changes in venous pressures and circulation time, the changes in blood distribution among the low and high pressure areas, and the physiological significance of the bradycardia when arterial pressure is markedly elevated primarily by an increase in total peripheral resistance [3] during global brain ischemia.

Central venous pressure (CVP) is not always useful as a parameter to assess the hemodynamics in the venous system for both clinical use and basic research, because CVP is usually controlled to maintain a constant pressure level by regulating the tone of the vessel walls and the output from the right ventricle [18]. In the present experiment substantial amounts of increase in CVP and FVP were elicited by brain ischemia. This result suggests that the regulatory mechanism for keeping CVP constant cannot compensate the hemodynamic changes in the venous system during brain ischemia. The pressure gradient in the venous system (PG) described by Guyton [14] is theoretically a major determinant of the rate at which blood flows into the heart although it is not highly quantitative to analyze venous return. This concept helps to explain, for example, why an increase in the right atrial pressure reduces venous return, because an increase in the right atrial pressure obviously decreases the venous pressure gradient. Therefore, changes in venous pressures during brain ischemia provides a useful information to evaluate the hemodynamics in the venous system during brain ischemia. We measured the circulation time of the dye as an index of venous blood flow. The present study demonstrated that there was a linear correlation between the changes in PG and circulation time (CT) during brain ischemia. Thus, changes in CT will be also informative for an analysis of the venous flow during brain ischemia.

The venous pressure is determined mainly by three factors: compliance of vessel wall, intravascular blood volume, and the output from the right ventricle [18]. In brain ischemia, a muscle pump induced by grand mal-like convulsion and the increase in intrathoracic pressure evoked by apnea at an expiratory position may also increase the value of CVP. The strong excitation of the sympathetic nerve activity evoked by brain ischemia changes the characteristics of pressure volume relationship in the veins from that in a collapsible tube to an arterial-like tube [13, 18] as well as production of contraction of arterial smooth muscle. These vascular changes may acutely result in centralization of blood volume, which is suggested by an elevation of left atrial pressure and CVP [19].
Dampney et al. [2] showed that the pressor response and the reduction in ascending aortic flow during brain ischemia were not altered by aortic denervation. The denervation again did not significantly alter the pressor response in the present experiment. Mochizuki's experiment shows that several repetitions of brain ischemia did not affect the increase of CVP (Mochizuki, unpublished data). These findings suggest that the degree of constriction of the venous vessels evoked by brain ischemia is not markedly affected by aortic denervation and that the suppression of the increase of CVP is due to abolishment of the bradycardia. During brain ischemia, the values of CVP, but not of FVP, showed a negative correlation with HR, and the PG showed a positive correlation with HR. Furthermore, the increase of CVP and FVP, decrease of PG, and prolongation of circulation time evoked by brain ischemia were significantly suppressed by aortic denervation. Judging from these facts, the larger increase of CVP than that of FVP before aortic denervation is likely to be the effects of the bradycardia. This means that abolishment of the bradycardia decreases the blood pooled in the large veins by accelerating the right ventricular pump function. Therefore, an effect of the bradycardia is a relative suppression of so-called centralization of venous blood and prevents its overflow into pulmonary circulation. A slight increase in CVP still remained during brain ischemia after aortic denervation. This may relate to other factors such as muscle pump [19], an increase of intrathoracic pressure and hypoxic pulmonary vasoconstriction [20].

CPBV decreased in 5 rabbits which showed marked bradycardia, HR of which fell below 200 beats/min. Hayashi [19] postulated that an increase in blood volume in the pulmonary circulation may occur during brain ischemia. This discrepancy between the two results is likely to be caused by a difference in the experimental procedure. Hayashi measured the flow of the pulmonary artery and the ascending aorta by using an electromagnetic flowmeter in open-chested rabbits and speculated the above postulation from the difference between the pulmonary and ascending arterial flow. We measured intracardiac and intravascular blood volumes in the cardiopulmonary system with a dye-dilution technique in the closed chest condition. Thus, the difference between the two results may be affected by whether the flow of the coronary artery, intracardiac volume and extravascular fluid filtrated from pulmonary capillaries are included or not and whether thoracotomy was performed or not.

Safar and London [21] suggested that the dye filtrates into extravascular space and CBV is overestimated when it is measured using dye-dilution technique in hypertensive patients. The rate of dye filtration in hypertensive patients was found to be at least minute order [22]. Therefore, the effect of extravascular filtration on CBV during brain ischemia for 30 s may be a minimum. The origin of the increased CBV might be blood stored in the spleen and liver and released by the strong excitation of sympathetic nervous system [12, 18].

Gerová and Gero reported that the radii of the abdominal [23] and femoral arteries [24] increase when the elevation of arterial pressure is evoked by sympa-
thetic stimulation or clamping of both common carotid arteries. Hirooka et al. [25] recently reported that the increase in the aortic diameter in the rabbit is about 1% of the baseline value when the arterial pressure increases by 26% with norepinephrine. If the diameter of all arterial system increases by 5% homogeneously when arterial pressure is elevated by 100% of the value before brain ischemia, volume of the arterial system will increase by 10.3%, because volume increases proportionally to the square of the radius (cross-sectional area). The blood volume of the arterial system is about 15% of CBV under intact conditions [26]. From these assumptions, the increase in blood volume in the arterial system during brain ischemia is about 1.5% of CBV before brain ischemia. In the present experiment, CBV during brain ischemia increased by 3.7 ml/kg. This increase was 5.9% of CBV before brain ischemia. CPBV did not increase during brain ischemia. Thus, it seems that the increase in CBV occurs mainly in the large veins.

There are a few reports concerning the occurrence of pulmonary edema during intracranial hypertension [7–9] or during brain ischemia [20]. Campbell and Visscher [7] demonstrated that vagotomy decreases the degree of pulmonary edema during intracranial hypertension; however, Chen et al. [8] and Chen and Wang [9] suggested that vagotomy does not affect edema. Campbell et al. and Chen et al. assessed the degree of pulmonary edema by measuring weight of the lung removed after animals died. Thus, they could not assess the effect of bradycardia on the pulmonary circulation in the initial phase during intracranial hypertension. In our experimental model the decrease in the left ventricular minute output is hardly affected by the bradycardia, although the stroke volume of the left ventricle is affected [3], showing that determinant of pressor response and the initial decrease in the left ventricular output is mainly due to an increase in systemic vascular resistance. On the other hand, the decrease in output from the right ventricle during the brain ischemia will greatly depend on the bradycardia because the pulmonary vascular resistance does not increase as much as that of the systemic vascular resistance. Thus, the bradycardia observed in the initial phase of brain ischemia is a major determinant of the blood volume in the cardiopulmonary system, and it probably plays a role to keep the difference between the right and left ventricular output down to a minimum. This physiological significance may be applicable to the bradycardia which occurred in intracranial hypertension [7–9] and diving [10].

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REFERENCES


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