Regional Cerebral Blood Flow and Oxygen Consumption of the Canine Brain During Hemorrhagic Hypotension

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Summary

The sequential changes in systemic and cerebral hemodynamics, systemic and cerebral oxygen transport and consumption rates, and the regional blood flows (measured with 15 μm microspheres) to the cortical and subcortical brain tissues were determined in nine dogs subjected to graded hemorrhage (10 ml/kg x 4 at 15 min intervals). As hemorrhage progressed, both mean arterial pressure and cardiac output decreased progressively. In contrast to the systemic circulation, the mean cerebral blood flow (mCBF) was well maintained by cerebral vasodilation and the cerebral O₂ consumption rate (CMRO₂) increased during the first three stages of hemorrhage. At 40 ml/kg of hemorrhage, there were significant reduction in mCBF and CMRO₂ despite the increase in O₂ extraction, suggesting the occurrence of cerebral hypoxia and decompensation of the cerebral circulation. There were remarkable regional variations in the responses of regional cerebral blood flows (rCBF) to hypovolemia, resulting in a significant redistribution of cerebral blood flow. The fractions of cardiac output supplying the diencephalon (thalamus and hypothalamus), the brain stem (pons and medulla oblongata) and the cervical spinal cord increased after hemorrhage up to 40 ml/kg. The redistribution of rCBF favors those areas where neurons related to cardiovascular control are located. These findings have significant implications relating to hemodynamic regulation during hemorrhagic hypotension.

Methods

The experiments were performed on nine mongrel dogs weighing 15–19 kg. Anesthesia was induced with pentobarbital (30 mg/kg, i.v.) which was supplemented at a rate of approximately 2 mg/kg/hr (i.v.). Pencur-
onium bromide (0.2 mg/kg, i.v.) was given for muscle relaxation. The dog was ventilated mechanically through a cuffed endotracheal tube with a fixed tidal volume (20 ml/kg) and the respiratory rate was adjusted to maintain the arterial CO₂ tension (P_aCO₂) at 35–42 mmHg. Following hemorrhage, especially when the volume bled exceeded 20 ml/kg, the respiratory rate had to be increased in order to maintain a relatively constant P_aCO₂. A low flow of oxygen (500 ml/min) was added to the inspired gas in order to ensure an arterial oxygen tension (P_aO₂) greater than 90 mmHg.

The esophageal temperature was monitored with a thermister coupled to a telethermometer (Yellow Springs Instrument Co., Yellow Springs, OH) and was kept between 37 and 38°C with electric heating pads. The left ventricle, the lower abdominal aorta and the pulmonary artery were catheterized through femoral arteries and veins. The superior sagittal sinus was cannulated through a midline trephination. The dogs were then heparinized (1000 U/kg initially and 500 U/kg hourly). All pressure measurements were made with the use of Statham transducers and a Grass polygraph recorder.

**Measurement of Blood Flow**

The cardiac output (CO) and regional cerebral blood flows (rCBF) were measured with radioactivity labeled 15-μm microspheres (New England Nuclear Corp., Boston, MA). The microspheres were supplied as suspensions in 10 percent dextran solution (M.W. 78,000) and were thoroughly examined with respect to the status of aggregation, presence of fragmentation, specificity of radionuclides and specific activity. Microspheres labeled with five different nuclides (⁵⁷Co, ¹¹⁵Sn, ¹⁰³Ru, ⁶⁸Nb and ⁴⁶Sc) were used, thus allowing five flow measurements in each dog. Detailed procedures for the preparation of the microspheres and their injection have been reported elsewhere.⁸ ¹⁰ Approximately 2 × 10⁵ to 4 × 10⁵ spheres per kg body weight were used for each measurement. The suspension of microspheres was injected into the left ventricle over a period of approximately 5 min. Fifteen min were allowed for the mixing to be complete and the vascular hindrances in the overall systemic (Zs) and cerebral (Zc) circulations were calculated by the use of a mini-computer (PDG-11/10, Digital Equipment Corp., Maynard, MA). The cardiac output (CO, in ml/min⁻¹) and the regional blood flow in each tissue (rBF, in ml-min⁻¹·100 gm⁻¹) were calculated with the use of the following equations:

\[
\text{CO} = \frac{A_i}{(A_i/Q_i)} \quad (1)
\]

\[
\text{rBF} = C_i/(A_i/Q_i) \quad (2)
\]

where A_i is the total radioactivity injected, A_i is the radioactivity of the arterial reference flow sample, Q_i is the reference flow withdrawing rate, and C_i is the radioactivity per 100 gm of tissue specimen. The mean cerebral blood flow (mCBF) was then calculated from the weighted mean of the rCBF in various regions of the brain.

Since the brain was dissected according to the anatomical locations, the weight of the tissue specimen varied considerably. Most of the regions were dissected into 1–1.5 gm specimens and the estimated number of microspheres in these regions was between 600 to 1,200 per specimen. Small tissues, e.g. pituitary gland and choroid plexus, weighed 50–80 mg, and the number of microspheres was estimated to be between 200 and 600 in these specimens.

**Experimental Protocol**

Following the surgical preparation and catheterization, a control measurement of regional blood flows and hemodynamic functions was made during the normovolemic state. The animal was then subjected to four steps of graded hemorrhage. Each step of hemorrhage was performed by withdrawing 10 ml/kg body weight of blood from the arterial catheter over a period of approximately 5 min. Fifteen min were allowed for hemodynamic stabilization before making measurements at that level of hypovolemia. The blood samples drawn for various measurements was immediately replaced with an equal volume of donor blood.

**Calculations of Flow Resistance and Vascular Hindrance**

The flow resistances in the overall systemic (R_s) and cerebral (R_c) circulations were calculated from the pressure-flow ratios. The resistance to flow is a function of the viscosity of blood (η) as well as the geometric hindrance of blood vessels (Z). In order to evaluate the relative contributions of these two factors to the flow resistance, arterial blood samples were also taken for viscosity determination at each level of hemorrhage. The viscosity of blood was measured with the use of an air-bearing coaxial cylinder viscometer¹¹ at 37°C and over a shear rate range from 0.5 to 200 sec⁻¹. The blood viscosity measured at a shear rate of 200 sec⁻¹ was used as the η value in the control state. As the blood flow decreased during hemorrhage, the effect of low shear rate on the η value was corrected by assuming that the shear rate change is proportional to the flow ratio.¹² The blood viscosity corresponding to this corrected shear rate was used as η in hypovolemic states. The vascular hindrances in the overall systemic (Z_s) and cerebral (Z_c) circulations were calculated by dividing the blood viscosity (η) into the respective flow resistances (R).
Determinations of Oxygen Transport and Utilization

During each level of hypovolemia, the pH, PO2, and PCO2 of the arterial, mixed venous (obtained from the pulmonary artery) and cerebral venous (obtained from the superior sagittal sinus) blood were determined with a blood gas analyzer system (Model 213, Instrumentation Laboratory, MA). The hemoglobin concentration (Hb, in gm/dl) and the oxygen saturation (S, in percent) were measured by the use of a CO-oximeter (Model 182, Instrumentation Laboratory). The hematocrit was determined by microcentrifugation and the plasma protein concentration (in gm/dl) was measured by refractometry. The oxygen content (in ml/dl of blood) was calculated as the sum of the hemoglobin-bound (0.0134 x Hb x S) and physically dissolved (0.003 x PO2) components for the arterial (AO2) and venous blood (VO2). The systemic and cerebral oxygen transport and consumption rates were calculated from cardiac output, mCBF, AO2 and (A - V)O2. The oxygen extraction ratio was computed as the ratio of (A - V)O2 to AO2.

Statistical analysis of the results obtained in various stages of hemorrhage was accomplished by analysis of variance (ANOVA) and the Student-Newman-Keuls (SNK) method of multiple comparison. A confidence level of 95 percent (p < 0.05) was considered statistically significant. All data reported in the Results section are mean ± SEM.

Results

Hemodynamic Functions

In the control normovolemic period, the mean arterial pressure (MAP) and sagittal sinus pressure (SSP) were 121.3 ± 8.2 mmHg and 10.7 ± 1.4 mmHg, respectively. With increasing amounts of hemorrhage, MAP decreased progressively and significantly (fig. 1a). At 40 ml/kg of hemorrhage, the MAP decreased by about 60 percent of control to 49.1 ± 6.7 mmHg. The SSP, on the other hand, remained relatively constant during the three stages of hypovolemia but decreased significantly by about 25 percent to 7.6 ± 1.2 mmHg at 40 ml/kg of hemorrhage.

During hypovolemia, the cardiac output (CO) was reduced progressively from 106.8 ± 9.9 ml/min-1 kg-1 in the control period to 38.7 ± 4.9 ml/min-1 kg-1 at 40 ml/kg of hemorrhage (fig. 1b). The decrease in CO following hemorrhage was primarily due to the reduction of stroke volume. In the control period, the heart rate was 162.2 ± 8.5 min-1 and the stroke volume was 10.6 ± 1.2 ml. At 20 ml/kg of hemorrhage, the stroke volume decreased significantly by about 25 percent while the heart rate remained constant. With increasing amounts of hemorrhage, the heart rate began to increase and the stroke volume decreased further. At 40 ml/kg of hemorrhage, the heart rate increased by about 33 percent while the stroke volume decreased by about 70 percent of their respective control values.

In the control period, the mean cerebral blood flow (mCBF) was 49.5 ± 5.3 ml/min-1.100 gm-1. In contrast to the reduction in CO, the mCBF showed a trend of increasing during the first stages of hemorrhage (fig. 1b), but the changes were not statistically significant. When hemorrhage progressed to 40 ml/kg the mCBF decreased significantly by about 40 percent below the control values.

Flow Resistance, Blood Viscosity and Vascular Hindrance

The changes in flow resistances in the systemic and cerebral circulations are shown in figure 2a. In the control period, the systemic flow resistance (SFR) was 1.24 ± 0.15 mmHg-ml-1-min-1-kg and the cerebral flow resistance (CFR) was 0.26 ± 0.05 mmHg-ml-1-min-1-kg. At 10 ml/kg of blood loss, there was no significant change in CFR. As hemorrhage increased from 10 to 30 ml/kg, CFR decreased progressively and significantly by 42 percent below the control values. At 40 ml/kg of hemorrhage, CFR slightly rose toward its control values. The SFR, though slightly elevated, did not show statistically significant change from the control values at all stages of hypovolemia.

In the control period, the blood viscosity was 4.5 ± 0.2 cP, the hematocrit (Hct) was 44.2 ± 1.6 percent and the plasma protein concentration (PPC) was 5.9 ± 0.5 gm/dl. At 10 ml/kg of hemorrhage, there was a slight but significant increase of Hct to 46.0 ± 1.4 percent and the PPC remained constant. As hemorrhage increased to 40 ml/kg, however, both Hct and PPC decreased by about 10 percent below their respective control values. As a result, the blood viscosity decreased during hemorrhagic hypovolemia (fig. 2b) despite the general reduction in shear rate as estimated from the changes of cardiac output (fig. 1b). At 30 and 40 ml/kg of hemorrhage, the blood viscosity decreased...
Changes of flow resistance (R, panel A), blood viscosity (η, panel B) and vascular hindrance (R/η, panel C) during various stages of hypovolemia. Values are mean ± SEM. Open circles connected with dashed lines are values for the systemic circulation. Closed circles connected with solid lines are values for the cerebral circulation. The asterisk symbols indicate significant difference from the control values (p < 0.05).

significantly by about 10 percent below the control values.

The changes in vascular hindrance, which reflects the magnitude of vasoconstriction or vasodilation contributing to the alterations of flow resistance, are shown in figure 2c. The cerebral vascular hindrance (CVH) decreased significantly by about 20 and 40 percent of the control values at 20 and 30 ml/kg of hemorrhage, respectively. The decrease in CVH indicates the occurrence of cerebral vasodilation at these stages of hypovolemia. At 40 ml/kg of hemorrhage, however, the decrease in CVH was only about 20 percent below the control values, indicating a lesser degree of vasodilation in the cerebral circulation as compared to 30 ml/kg of hemorrhage. In contrast to the response of CVH, the systemic vascular hindrance (SVH) rose slightly, although the change was not statistically significant at all stages of hypovolemia (fig. 2c).

Oxygen Transport and Consumption Rates

The control systemic and cerebral O₂ transport rates were 19.9 ± 1.5 ml-min⁻¹·kg⁻¹ and 9.4 ± 1.1 ml-min⁻¹·100 gm⁻¹, respectively. As the CO decreased, the systemic O₂ transport rate (STRO₂) decreased progressively during hypovolemia (fig. 3a). At 40 ml/kg of hemorrhage, STRO₂ decreased to about 30 percent of the control values. In contrast, the cerebral O₂ transport rate (CTRO₂) remained relatively constant during the first three stages of hypovolemia, but it decreased significantly to about 65 percent of the control values at 40 ml/kg of hemorrhage.

In the control period, the oxygen consumption rates of the systemic and cerebral circulations were 4.1 ± 0.3 ml-min⁻¹·kg⁻¹ and 3.5 ± 0.6 ml-min⁻¹·100 gm⁻¹, respectively. During the first three stages of hypovolemia, the cerebral O₂ consumption rate (CMRO₂) increased progressively to about 160 percent of the control values at 30 ml/kg of hemorrhage. When hemorrhage progressed to 40 ml/kg, CMRO₂ decreased and returned to the control level (fig. 3b). The systemic O₂ consumption rate (SMRO₂), on the other hand, remained relatively constant at all stages of hypovolemia studied.

The control oxygen extraction ratio of the cerebral circulation (CEO₂) was 0.38 ± 0.05, which is significantly greater than the value of 0.22 ± 0.03 found in the systemic circulation (SEO₂). During hypovolemia, both SEO₂ and CEO₂ increased significantly (fig. 3c), but the increase of oxygen extraction was greater in the systemic than in the cerebral circulation. As hemorrhage progressed to 40 ml/kg, SEO₂ increased to 0.69 ± 0.05 (an increase of 0.47 over control) while CEO₂ rose to 0.65 ± 0.04 (an increase of 0.27). Despite the constancy of SMRO₂, the arterial blood pH decreased progressively from 7.36 ± 0.02 in the control period to 7.16 ± 0.04 at 40 ml/kg of hemorrhage.

Regional Cerebral Blood Flow Measurement

The control values of regional cerebral blood flows (rCBF) are shown in figure 4, together with those of blood flows to some intracranial extracerebral tissues

significantly by about 10 percent below the control values.
There were considerable variations in blood flow distribution among the regions studied. The averaged blood flow to the cerebral cortex was 48.3 ml-min⁻¹·100 gm⁻¹. Within the cerebral cortex, the blood flow to cortical gray matter was 50.4 while that to the cortical white matter was 27.3 ml-min⁻¹·100 gm⁻¹. The blood flows to the subcortical cerebral tissues ranged from 20.8 for the corpus callosum to 83.9 ml-min⁻¹·100 gm⁻¹ for the caudate nucleus, with the values for the diencephalon, brain stem and cerebellum being intermediate. The blood flows to the cervical spinal cord was 17.0 ml-min⁻¹·100 gm⁻¹ and that to the dura mater was 45.1 ml-min⁻¹·100 gm⁻¹. Among all tissues studied, the pituitary gland and the choroid plexus received the highest blood flows: 285.0 ml-min⁻¹·100 gm⁻¹ for the pituitary gland and 476.0 ml-min⁻¹·100 gm⁻¹ for the choroid plexus.

The responses of regional intracranial blood flows to graded hemorrhage are summarized in figure 5. In general, three distinct types of responses can be seen: those of the cerebral tissues, the non-cerebral tissues and the cervical spinal cord. During the first two stages of hemorrhage, the rCBF values to the cerebral tissues, including both cortical and subcortical regions, were relatively constant. At 30 ml/kg of hemorrhage, rCBF to the diencephalon (thalamus and hypothalamus) and the brain stem (pons and medulla oblongata) increased significantly above the control values, while it remained essentially constant in the cortical white matter, corpus callosum and caudate nucleus. The rCBF to the cortical gray matter and cerebellum showed a trend of increase, but the changes were not statistically significant. At 40 ml/kg of hemorrhage, rCBF to all cerebral tissues decreased significantly from the values obtained at 30 ml/kg of hemorrhage.

The rECBF to the choroid plexus and dura mater reduced progressively and significantly as hemorrhage progressed. At 40 ml/kg of hemorrhage, the choroidal blood flow decreased to 22 percent of control and the dural blood flow decreased markedly to a level as low as 7 percent of control. The blood flow to the pituitary gland remained constant during the first two stages of hemorrhage, but progressively decreased thereafter. At 40 ml/kg of hemorrhage, the blood flow to the pituitary gland decreased significantly to 36 percent of the control values. The blood flow to the cervical spinal cord did not show any significant change at all stages of hypovolemia.
Since the cardiac output decreased progressively during hypovolemia, the response of regional blood flows following hemorrhage was also related to the availability of overall blood supply. Figure 6 shows the changes of the fraction of cardiac output which supplies the regional blood flow to various tissues during different stages of hypovolemia. At 10 ml/kg and 20 ml/kg of hemorrhage, the rCBF/CO ratio for all cerebral tissues increased. The rECBF/CO ratio of the choroid plexus and dura mater decreased slightly from their respective control values, while that of the pituitary gland increased by 40 percent at 20 ml/kg of hemorrhage. At 30 ml/kg of hemorrhage, rCBF/CO ratio for all cerebral tissues further increased, while rECBF/CO ratio for choroid plexus and dura mater continued to decrease; the ratio for the pituitary gland decreased to its control values. When hemorrhage progressed to 40 ml/kg, rCBF/CO ratios for cerebral tissues showed remarkable regional variations. The rCBF/CO values for the diencephalon (hypothalamus and thalamus), brain stem (pons and medulla oblongata) and cervical spinal cord further increased to about 150 percent above their respective control values. The rCBF/CO ratios for the cortical gray matter and cerebellum remained at about 100 percent above their respective control values. The rCBF/CO ratios for the cortical white matter, corpus callosum and caudate nucleus decreased from the values obtained at 30 ml/kg of hemorrhage to about 50 percent above the control values. The rECBF/CO ratio for the choroid plexus and dura mater further decreased to 60 and 20 percent of control, respectively, while that for the pituitary gland remained at its control level at 40 ml/kg of oligemia.

Discussion

The notion that the cerebral circulation is capable to autoregulate during changing perfusion pressure is well known. Most of the investigations on autoregulation of the cerebral circulation are concerned primarily with the total or mean cerebral blood flow (mCBF). Our results showed that at the final stage of hemorrhage, when MAP was reduced to 50 mmHg, the cerebral circulation lost its ability to autoregulate as mCBF decreased significantly by about 40 percent of baseline value (fig. 1). This is in general agreement with the previous reports that the lower limit of autoregulation of the cerebral circulation is at a MAP of 65–70 mmHg. It should be emphasized, however, that the limit of autoregulation in relation to perfusion pressure was not studied systematically in the present investigation where the changes of cerebral blood flow were related to the magnitude of hypovolemia rather than the perfusion pressure. Therefore, a direct comparison of the present results with those of previous reports on autoregulation of cerebral circulation with perfusion pressure can not be rigorously made. It has been shown that the blood flow to the brain is non-homogeneously distributed. The results of the present study indicate not only that the distribution of cerebral blood flow is not uniform among various regions of the brain (fig. 4), but also that there are considerable regional variations of changes in cerebral perfusion during moderate hypotension even when the mCBF is well autoregulated (fig. 5). These findings suggest that the control of cerebral blood flow operates primarily on a regional basis. During hemorraghic hypotension, the CO decreases. The changes in regional cerebral perfusion in relation to overall hemodynamic adjustment during hypovolemia can better be appreciated by evaluating rCBF as a fraction of CO. Thus, the preferential distribution of CO to the thalamus, hypothalamus and brain stem areas occurred at 30 ml/kg of hemorrhage when mCBF remained constant. This pattern persisted and became even more prominent at 40 ml/kg of hypovolemia when autoregulation of mCBF failed (fig. 6). Therefore, the present results further suggest that the redistribution of regional cerebral perfusion during acute hemorrhage is a continuous process and is a function of the severity of hypovolemia and the resultant reduction in CO.

Several investigators have studied the response of regional cerebral blood flows (rCBF) using the microsphere technique during hemorraghic hypotension or shock condition. Since cerebral vasculature is sensitive to local PCO₂, the results would depend on the level of P₃CO₂, and hence the mode of ventilation. Studying the effect of hemorraghic hypotension (MAP = 55 mmHg) on dogs breathing spontaneously, Slater et al did not detect a redistribution of rCBF, as P₃CO₂...
decreased from about 33 to 27 mmHg due to hyperventilation during hypotension. The simultaneous development of hypoxia may have masked the effect of hypotension on rCBF redistribution. Experiments on acute hemorrhage in anesthetized dogs under controlled ventilation to maintain P(\text{CO}_2) have shown a similar redistribution of rCBF, as in the present study. Studies on cats with maintained P(\text{CO}_2), however, did not show a redistribution of rCBF during hypotension. This discrepancy may be attributable to the species difference. In unanesthetized dogs under spontaneous respiration and with P(\text{CO}_2) decreased to about 20 mmHg following hemorrhage (\text{MAP} = 69 \text{ mmHg}), Fritschka et al. found that the ratio rCBF/CO was significantly elevated in the thalamus, mesencephalon, pons and medulla after hemorrhage. Since a chronic ventriculocisternal system was used in this study to perfuse the cerebral ventricular system with a solution equilibrated with 5 percent CO\textsubscript{2} and 95 percent oxygen, the P(\text{CO}_2) of the cerebral interstitial fluid, which has been proposed to be the main factor in affecting CBF, was probably maintained at the normocapnia level, as in the present study.

In the present investigation, when hemorrhage progressed to 30 ml/kg, the oxygen consumption rate of the brain was found to be significantly increased while the cerebral oxygen transport rate remained constant (figs. 3a and 3b). The increased oxygen consumption at a constant oxygen transport rate was made possible by a compensatory increase in oxygen extraction by the brain tissues (fig. 3c). A similar increase in cerebral oxygen utilization following moderate hemorrhage has also been observed in baboons and in dogs. The mechanisms of increased cerebral oxygen consumption during hemorrhagic hypotension are not clearly understood. There is evidence that hemorrhage causes excitation of neurons responsible for cardiovascular regulation by changes in afferent impulses from reflexogenic areas in the circulation. The hyperexcitability of these neurons may lead to an increase in oxygen consumption. Hemorrhage also causes the release of various circulating vasoactive substances including catecholamines, vasopressin and renin-angiotensin. The catecholamines can cause an increase in cerebral oxygen consumption and blood flow rates, and angiotensin II can stimulate the sympathetic neurons in the brain. Recently, with the use of autoradiographic 14C-deoxyglucose technique, it has been demonstrated in rats that hemorrhagic hypotension (\text{MAP} 50–75 \text{ mmHg}) causes significant increases in glucose utilization in several nuclei located mainly in the medulla, pons and midbrain. These areas with a significant elevation in glucose utilization coincide with those regions where rCBF was found to be increased at 30 ml/kg of hemorrhage in the present study (fig. 5). Therefore, the redistribution of rCBF during hemorrhagic hypotension may be directly related to local increase in metabolic activity caused by the excitation of neurons regulating cardiovascular functions.

When hemorrhage progressed to 40 ml/kg the blood flow and oxygen transport rate to the brain decreased (figs. 3a and 3b). A reduction in cerebral oxygen consumption despite the further increase in oxygen extraction (fig. 3c) suggests the occurrence of cerebral hypoxia which would lead to cerebral dysfunction and development of irreversible shock syndrome. It has been shown that there are regional variations in the susceptibility to hemorrhagic shock among various parts of the brain. The neurons in the cerebral cortex were depressed before those in the hypothalamus, brain stem and spinal cord. The preservation of neuronal functions in the hypothalamus, brain stem and spinal cord may result from the preferential distribution of cardiac output to these regions following severe hypovolemia observed in the present study. The mechanism of this preferential redistribution of cardiac output in the brain at the late stage of hemorrhagic hypotension is unclear. There is increasing evidence for the existence of central neurogenic control of cerebral blood flow. Specific areas located in the pontine and midbrain reticular formations, the thalamus and the hypothalamus appear to influence cerebral blood flow and metabolism. It is interesting to note that the perfusion and function of these areas seem to be most preserved during hemorrhagic hypotension.

The severe reduction of blood flow to the intracranial non-cerebral tissues, e.g. dura mater and choroid plexus, further indicates the redistribution of cardiac output to the brain during hemorrhagic hypotension. The response of pituitary blood flow to hemorrhage as compared to cerebral tissues is of special clinical implication. It is known that panhypopituitarism (Sheehan's syndrome) can occur as a result of postpartum pituitary necrosis. This syndrome, which is characterized by various symptoms and signs of hormonal disturbances in the puerperium, is usually associated with uterine hemorrhage during delivery. It occasionally develops after a bout of hypotension without a large amount of blood loss. The results of the present study suggest that the less well maintained pituitary blood flow during hemorrhagic hypotension may preferentially cause pituitary dysfunction without any other neurological deficits.

In summary, the present investigation demonstrated that there were regional variations in response to hemorrhagic hypotension, resulting in a significant redistribution of cerebral blood flow such that proportionately more cardiac output supplying the diencephalon (thalamus and hypothalamus), the brain stem (pons and medulla oblongata) and the cervical spinal cord. This pattern of redistribution of regional blood flow persisted even when the mean cerebral blood flow decreased following further hemorrhage to 40 ml/kg. The redistribution of regional cerebral blood flow seems to favor those areas where neurons related to cardiovascular control are located. These findings have significant implications relating to hemodynamic regulation during hemorrhagic hypotension.

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References
Regional cerebral blood flow and oxygen consumption of the canine brain during hemorrhagic hypotension.

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