

Spinal cord blood flow in dogs: the effect of blood pressure

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SUMMARY A study has been made into the effects of blood pressure on the spinal cord blood flow. Under conditions of normoxia and normocarbica a well-functioning autoregulation was present between 150-60 mmHg. Below 60 mmHg the flow decreased with reductions in pressure. In individual dogs, autoregulation was sometimes present to 40 mmHg. Under conditions of hypoxia or hypercarbia, autoregulation was absent or severely impaired. The results are discussed in relation to the cerebral circulation and to some aspects of experimental cord disease.

The effect of arterial blood pressure on cerebral blood flow (CBF) in dogs has been studied extensively. Early investigations were concerned with the observed response of pial vessels to changes in pressure (Fog, 1938). Since then, numerous studies have demonstrated that, under conditions of normoxia and normocarbica, the CBF remains unchanged, despite wide variations in blood pressure (Rapela and Green, 1964; Harper, 1965; Ekstrom-Jodal, Haggendal and Nilsson, 1970). A limited number of studies have been made into the effects of blood pressure on the spinal cord blood flow (SCBF). Otomo *et al.* (1960) directly observed the response of spinal vessels to pressure changes and Kindt (1971) used a heat clearance method to study the effects of noradrenaline induced hypertension in monkeys.

This paper examines the response of SCBF to changes in arterial pressure under conditions of normoxia and normocarbica. In addition, the effects of blood pressure under conditions of hypercarbia or hypoxia have been studied. These are states in which spinal vasodilatation occurs with a resultant increase in SCBF (Griffiths, 1973b). The cerebral autoregulation is known to be impaired under these conditions and it would be useful to know if the spinal circulation reacted similarly.

METHOD

Twenty-five unselected dogs were used, 11 for the effects of hypotension at normocarbica and normoxia (group A), eight at normocarbica and hypoxia (group B), and six at normoxia and hypercarbia (group C). Seven of the normoxic, normocarbica group were induced with thiopentone (25 mg/kg) and maintained on 0.5% halothane in a 70% nitrous oxide oxygen mixture, while the others were anaesthetized with pentobarbitone (25 mg/kg) and maintained on the N₂O/O₂ mixture. The dogs in the other two groups were all anaesthetized with pentobarbitone. The gas mixture was delivered through a Palmer pump with ventilation adjusted to maintain normocarbica during surgical preparation. A femoral artery was cannulated and the mean arterial blood pressure measured with a damped mercury manometer. This cannula also allowed collection of arterial samples for blood gas analysis. During each estimation, blood pH, paco₂, and paO₂ were measured using standard electrodes.² Any base deficit was corrected with 8.4% sodium bicarbonate. The PCV was measured using the microhaematocrit method and the result used in the selection of λ (tissue/blood partition coefficient). The pharyngeal temperature was measured with a mercury thermometer and heating lamps were used to maintain the temperature between 37-38° C.

Dorsal laminectomies were performed to expose the required cord segments (T12/T13) with the dura intact. A control measurement was made under conditions of normoxia, normocarbica, and normo-

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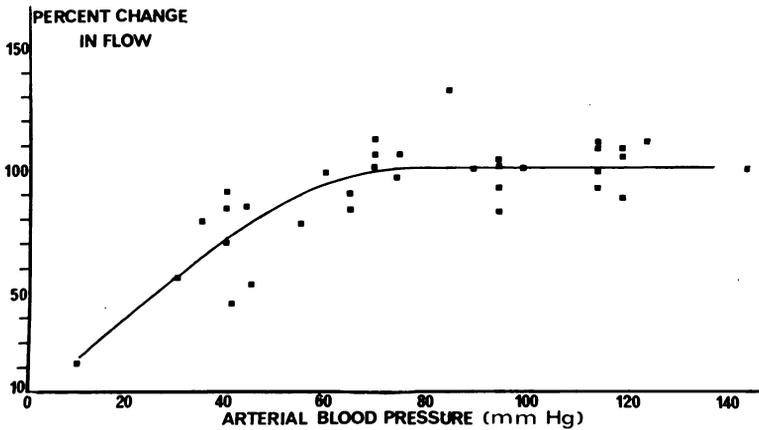


FIG. 1. The effect of hypotension on SCBF under conditions of normoxia and normocarbica. The combined results from eight dogs are shown. The SCBF at 95 mmHg was taken as 100%.

tension. In the dogs of group A the blood pressure was then decreased as described below. In dogs of group B, hypoxia was induced by increasing the percentage of N₂O in the inspired gases until the p_aO₂ was 30–45 mmHg. A second measurement was made at normotension to ensure that the SCBF had increased by the expected amount and the blood pressure was then reduced as described below. In dogs of group C, hypercarbia was produced by adding CO₂ to the inspired mixture until the p_aCO₂ was 85–100 mmHg. A second measurement was made at normotension to ensure that the expected vasodilatation had occurred. The blood pressure was then reduced.

Graded hypotension was produced by bleeding the dog, via the femoral cannula, into a reservoir. The SCBF was determined at least 10 minutes after the pressure had stabilized. In three dogs of group A,

a large diameter cannula was inserted directly into the caudal aorta through a laparotomy incision. During a clearance to measure SCBF, the blood pressure was reduced rapidly by bleeding via this cannula.

The clearance of ¹³³Xe after direct injection into the spinal cord was monitored with an uncollimated scintillation counter coupled through a ratemeter to a linear recorder. The clearance curve was transposed onto semilogarithmic paper for the calculation of T_{1/2}.

The blood flow was calculated from the formula—

$$SCBF \text{ (ml./100 g/min)} = \frac{\lambda \times \log_e 2 \times 60}{T_{1/2}} \times 100$$

Full details of the technique have been presented in a previous paper (Griffiths, 1973a).

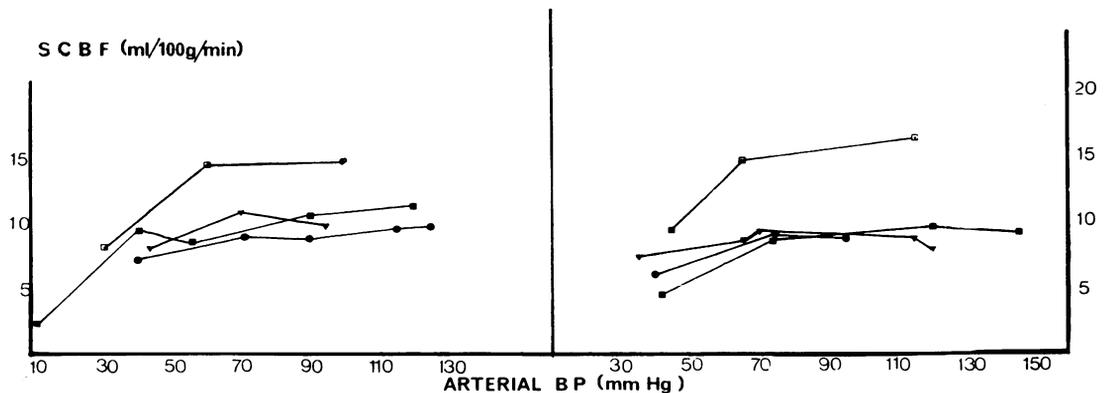


FIG. 2. The effect of hypotension on absolute SCBF in eight dogs under conditions of normoxia and normocarbica.

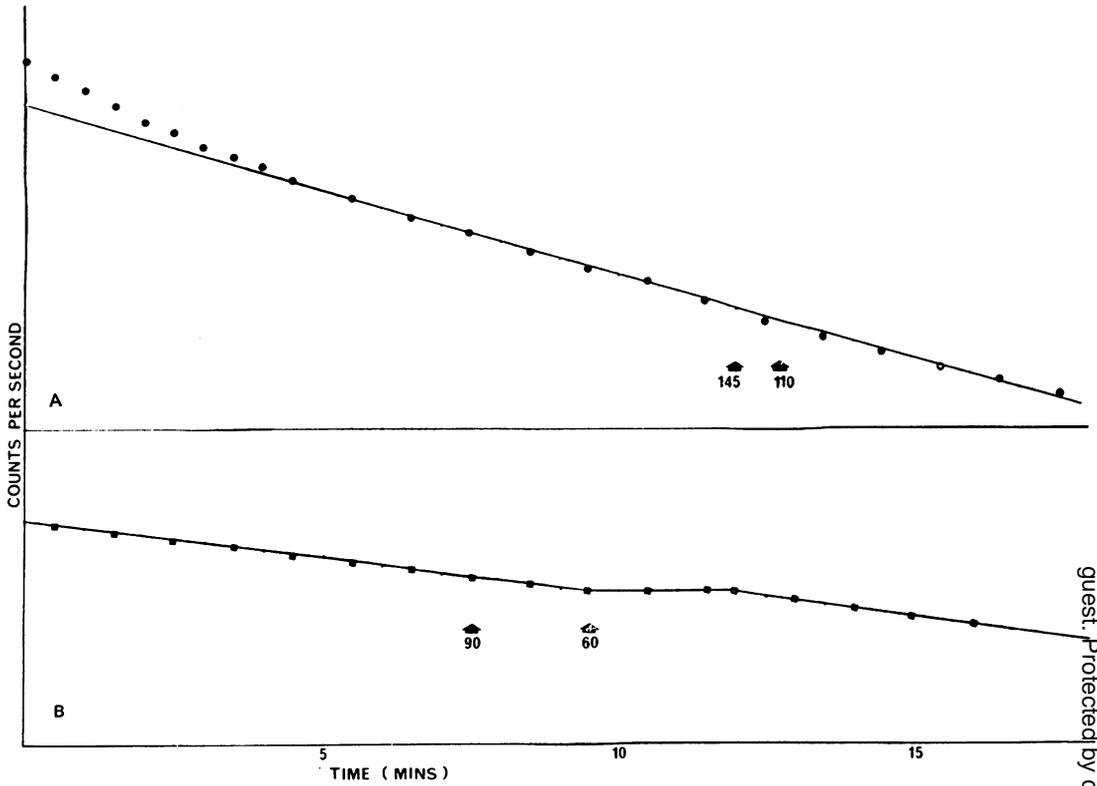


FIG. 3. Semilogarithmic plots of two clearance curves from the same dog. A. demonstrates a biexponential clearance curve during the slow component of which the blood pressure is reduced from 145 to 110 mmHg over a period of 45 sec (arrows). B. shows a monoexponential clearance during which the blood pressure is reduced from 90–60 mmHg over a period of 2 min. (arrows).

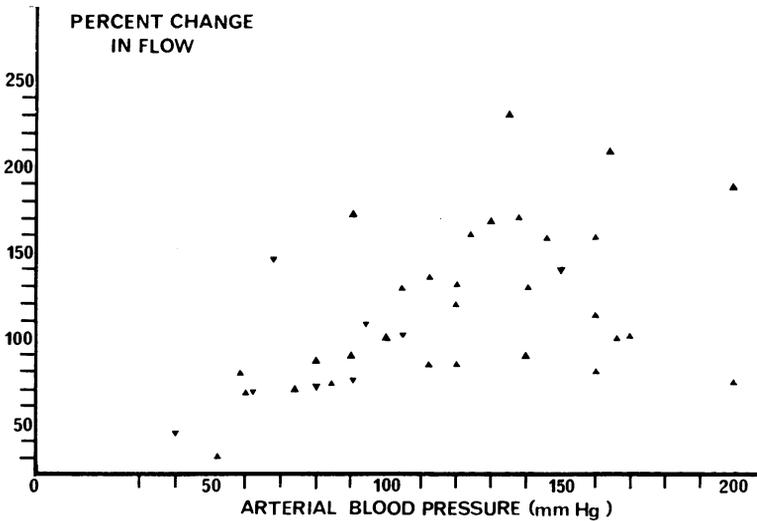


FIG. 4. The effect of hypotension on SCBF under conditions of hypoxia and normocarbida. The combined results from eight dogs are shown. The SCBF at 100 mmHg was taken as 100%.

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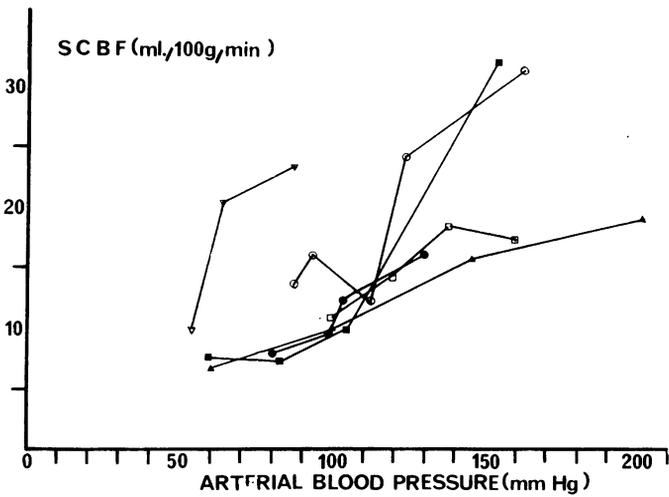


FIG. 5. The effect of hypotension on absolute SCBF in six dogs under conditions of hypoxia and normocarbica.

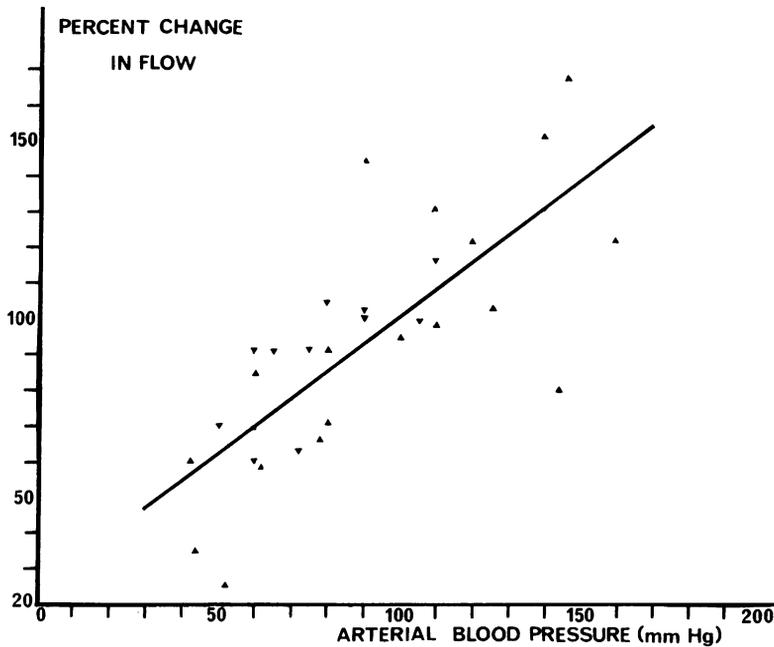


FIG. 6. The effect of hypotension on SCBF under conditions of normoxia and hypercarbica. The combined results from six dogs are shown. The SCBF at 90 mmHg was taken as 100%.

RESULTS

GROUP A: NORMOXIA AND NORMOCARBIA The percentage change in flow with progressive hypotension is presented in Fig. 1 and the absolute changes in flow are shown in Fig. 2. Variations in blood pressure between 150 and approximately 60 mmHg did not significantly alter the flow.

Below 60 mmHg the flow decreased with reduction of pressure.

In the three dogs where pressure was decreased rapidly during a clearance, no change in the slope of the curve was evident between 180 and approximately 100 mmHg. Below 100 mmHg a decrease in the clearance rate was noted, after the rapid exsanguination. Figure 3

demonstrates two clearances in the same dog at different initial arterial pressures.

GROUP B: HYPOXIA AND NORMOCARBIA Figure 4 shows the effect of hypotension on blood flow in a situation where hypoxia caused a marked vasodilatation. The percentage change in SCBF for eight dogs is shown. There is a wide scatter in points, especially at higher pressures, but a linear correlation between the flow change and pressure was present ($r=0.667$, $P<0.001$). The changes in absolute blood flow during hypotension are shown in Fig. 5. These results show that, in general, the SCBF falls progressively with reductions in blood pressure, although in two dogs autoregulation was present above a blood pressure of 110 mmHg.

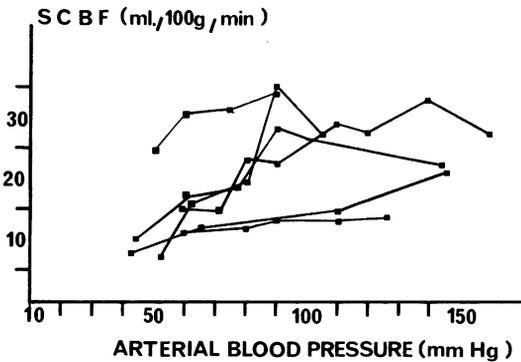


FIG. 7. The effect of hypotension on absolute SCBF in six dogs under conditions of normoxia and hypercarbia.

GROUP C: HYPERCARBIA AND NORMOXIA Figure 6 shows the percentage change in SCBF, in hypotension where the vessels are dilated due to hypercarbia. There is a linear correlation ($r=0.749$, $P<0.001$). The changes in absolute blood flows are shown in Fig. 7. Again the blood flow decreases with the blood pressure, although in some dogs a limited form of autoregulation is shown at higher pressures.

DISCUSSION

It is evident from Figs 1 and 2 that at normoxia and normocarbida the blood pressure may be

altered between 150 and approximately 60 mmHg without causing a significant change in blood flow. This is the phenomenon known as autoregulation. It is apparent from Fig. 2 that autoregulation can occur to arterial pressures of about 40 mmHg in some dogs. Autoregulation has been repeatedly demonstrated in the canine cerebral circulation (Harper, 1965; Rapela and Green, 1964; Häggendal and Johansson, 1966). Before these quantitative studies, direct observation of the pial vessels had shown dilatation in response to hypotension and constriction to hypertension (Fog, 1938). Kindt (1971) demonstrated autoregulation to increasing blood pressure, induced by noradrenaline, in the cervical cord of monkeys. He further showed that this feature was retained after high cervical cord transection. Otomo *et al.* (1960) noted no change in cord pial vessel diameter until the blood pressure had fallen by about 20%. They suggest that blood pressure is the chief factor controlling blood flow and oxygen tension in the cord. The present experiments (hypotension) and those of Kindt (1971) (hypertension) do not support these findings.

Autoregulation allows normal functioning of the brain energy metabolism to markedly reduced arterial pressures. Siesjö *et al.* (1973) measured brain concentrations of ATP, ADP, AMP, and creatine phosphate in rats made progressively hypotensive. No significant change in any of these metabolites was found until the arterial pressure dropped to 35 mmHg. These experiments also suggest that autoregulation is not a result of gross impairment of brain energy metabolism.

The failure of rapid exsanguination, above a pressure of 100 mmHg, to alter the clearance curves also supports the concept of autoregulation. It is likely that some temporary decrease in flow does occur but the technique employed in this study is not designed to measure transient changes in flow and, provided the flow rapidly returns to its former value, no decrease in the slope will be seen. Rapela and Green (1964) found that the CBF returned to normal approximately 30 seconds after the common carotid arteries were clamped.

The situation is changed somewhat in hypercarbia or hypoxia. The present experiments suggest that in both cases autoregulation tends to be

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abolished, although in both hypercarbia and hypoxia some degree of autoregulation was found in occasional dogs. Partial autoregulation occurred only at higher pressures and was never seen below about 90–100 mmHg. This autoregulatory tendency at higher pressures probably accounts for the scatter in Fig. 4.

Harper (1965) found a linear relationship between CBF, and arterial pressure at hypercarbia. He suggests that, with the vasodilatation due to hypercarbia, the vessels are unable to dilate further with a falling blood pressure. He supports this theory by presenting the effects of CO₂ on CBF at hypotension, where, at a pressure of 50 mmHg, hypercarbia and hypocarbia had little or no effect on CBF.

There is not universal agreement on these topics. Häggendal and Johansson (1966) found a significant but reduced increase in CBF in hypercarbic hypotensive (BP 60 mmHg) dogs and showed autoregulation persisting at higher blood pressures. Ekström-Jodal *et al.* (1970), in further studies, confirmed their findings that autoregulation did occur with vasodilatation due to CO₂ and papaverine. The results from the present experiments when examined in total (Fig. 6) tend to support the linear correlation, although individual dogs did show autoregulation at higher pressures.

Raichle and Stone (1972) investigated the effect of hypercarbia on CBF in rhesus monkeys which were exposed to 6, 9, and 12% CO₂. With increasing CO₂ levels, autoregulation was present only at higher blood pressures, until at 12% CO₂, it could not be demonstrated. The animals were then placed in a sealed environment chamber at 6% CO₂ for five days. The CSF pH was normal after this time, due to a rise in the bicarbonate ion. When autoregulation was tested at 6% CO₂ it was found to be identical with that at normocarbia and a degree of autoregulation was shown at 12% CO₂. This latter finding suggests that the loss of autoregulation in acutely hypercarbic animals is due to a decrease in perivascular pH.

Hypoxia is known to abolish or impair cerebral autoregulation (Freeman and Ingvar, 1968). Häggendal and Johansson (1966) found that, when the arterial oxygen saturation was reduced to less than 60%, a passive pressure-flow relationship developed. In a later study Ekström-Jodal *et al.* (1969a) found a functioning auto-

regulation at marked arterial hypoxia (oxygen saturation 40%) in some dogs.

In the present studies, autoregulation tended to be abolished at arterial oxygen tensions of between 30 and 45 mmHg. However, in two dogs, autoregulation was present at higher arterial pressures (above approximately 110 mmHg).

It is evident that at normoxia and normocarbia the spinal cord of the anaesthetized dog demonstrates a well-functioning autoregulation. At both hypercarbia and hypoxia this tendency is impaired. Why certain dogs show partial retention of autoregulation at higher pressures is, at present, unknown. The mechanism promoting cerebral autoregulation is also unknown. At present the two main hypotheses are concerned with metabolic and myogenic factors. The myogenic theory implies that changes in transmural pressure lead to alterations in vasomotor tone, while the metabolic theory suggests that alterations in tissue pH after the reduction in perfusion pressure are responsible for the changes in vascular calibre.

Ekström-Jodal *et al.* (1969) presented evidence in favour of the myogenic theory. This was based on the presence of autoregulation at hypocarbia and hypercarbia (this is not universally accepted) and the failure of autoregulation when the perfusion pressure was reduced by increasing the central venous pressure. Symon *et al.* (1971) also support the myogenic nature of autoregulation. They increased the pressure in branches of the middle cerebral artery by direct injection of fluid and measured the venous outflow from the brain with flowmeters. Using this system, they found a functioning autoregulation at arterial pCO₂ of 60–70 mmHg and a short latency of response to the pressure increments (<2 sec). Autoregulation was, however, abolished by hypoxia.

The work of Raichle and Stone (1971) and Harper (1965), which has been previously described, suggests that metabolic factors are of importance and this view is also taken by Rapela and Green (1964). The problem, however, is far from settled.

Autoregulation may also be abolished by disease or trauma. Reivich *et al.* (1969) demonstrated loss of autoregulation in cats' brains, which had been traumatized by a jet of com-

pressed nitrogen. This point illustrates the necessity for atraumatic methods in blood flow measurement. In the direct injection technique (as in the present study) the trauma caused by the needle is obviously minimal, as autoregulation is not abolished. Palleske (1969) produced cord oedema with a cold injury and demonstrated loss of SCBF autoregulation. The flow passively followed changes in blood pressure.

Detailed studies of SCBF in disease have yet to be made, but it is quite probable that in acute trauma autoregulation will be impaired as in the hypercarbic or hypoxic dogs.

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