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A COMPARATIVE STUDY OF MIDDLE CEREBRAL PRESSURE IN DOGS AND MACAQUES

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SUMMARY

1. A comparison has been made of the pressures recorded from pial branches of the middle cerebral artery in dogs and macaques. This pressure has been shown to be between 88 and 95 % of femoral arterial pressure in dogs under chloralose anaesthesia, and between 80 and 90 % of femoral arterial pressure in macaques similarly anaesthetized.

2. The effect of occlusion of the main vessels in the neck is shown to differ considerably in the two species. Blood pressure within the forebrain of the dog is shown to be largely dependent upon the integrity of the external carotid artery, whereas in the monkey the external carotid artery is without effect in the maintenance of forebrain blood pressure. Occlusion of the four major arteries in the neck is shown to produce a greater effect in the macaque and to be accompanied by signs of medullary ischaemia in this species.

3. After occlusion of the main middle cerebral artery, arterial pressure measured distal to the occlusion depends upon the integrity of collateral vessels from the other cerebral arteries. When only a branch of the middle cerebral artery is occluded, the greater part of the residual blood pressure depends upon anastomoses from other branches of the middle cerebral artery itself.

INTRODUCTION

Collateral channels have been described both in the dog and macaque which in a varying percentage of animals are capable of ensuring the animal's survival after occlusion of either the vertebral or the carotid arteries in the neck (Cooper, 1836; Andreyev, 1935; Donald & White, 1961). Within the skull, other collateral channels in the leptomeninges have been shown to function within a few minutes of occlusion of a major cerebral vessel (Petersen & Evans, 1937; Symon, 1960, 1961). They have been found responsible for the restoration of blood flow within the territory

of an occluded cerebral artery sufficient to prevent infarction (Thompson & Smith, 1951; Meyer, 1958) or to reduce it under certain circumstances (Rosomoff, 1956, 1957).

The present experiments were designed to compare the pressures in the leptomeningeal branches of the middle cerebral artery of two species, the dog and macaque, after occlusion of various vessels in the neck, and of the middle cerebral artery itself. The two species chosen are those commonly employed in experimental work on the cerebral circulation. Because the anatomy of the cerebral vessels in the two species is different, it seems important to establish the degree to which the collateral circulation maintains the pressure in the middle cerebral artery after occlusion of major vessels in the neck.

METHODS

Fifteen dogs weighing between 15 and 30 kg and six *Macacus* rhesus monkeys weighing between 5 and 8 kg were used. Twelve dogs were anaesthetized with chloralose (100 mg/kg) after induction with either thiopentone sodium (25 mg/kg I.V.) or ethyl chloride/ether by inhalation. Three dogs were maintained on thiopentone sodium throughout. In the monkeys, anaesthesia was induced with thiopentone 20 mg/kg and maintained with chloralose 60 mg/kg. Previous experience (Symon, 1961) has shown that prolonged thiopentone anaesthesia in the monkey is unsatisfactory.

Blood pressure was recorded by mercury manometer from the femoral artery. A clear airway was maintained by a cuffed endotracheal tube.

The carotid and vertebral vessels were exposed in the neck as described previously (Symon, 1961). Occlusion of a carotid artery was preceded by section of the carotid sinus nerve to diminish changes in arterial blood pressure. The small branches at the carotid bifurcation in both species were preserved as far as possible, although the ascending pharyngeal artery in the dog was occasionally ligated. Occlusion of the vessels in the neck was by bulldog clip.

Cannulation of vessels on the pial surface. After opening the dura, the exposed brain was covered with a pool of artificial c.s.f. (Merlis, 1940). Under a dissecting microscope, the arachnoid membrane surrounding a suitable branch of the middle cerebral artery was dissected away from the vessel, and two fine threads were placed beneath the vessel so that it could be suspended between the gently tightened threads (Fig. 1). The vessel was then opened, and a fine catheter of tip external diameter 250–400 μ introduced and tied in place. In some experiments, two catheters were introduced into the same vessel, one towards and one away from the heart.

Pressure within the small cannulated vessels was recorded by a pressure sensitive transducer (Statham gauge, Type P 23 Db), the output of which passed through an amplifier (Southern Instruments M.R. 501) to a pen recorder (Leeds & Northrup, Type 400).

At the beginning and end of each experiment, the catheter, Statham gauge and slow recorder were calibrated against a mercury manometer in an air-filled system. Over the course of 8 or 9 hr, the usual length of experiment, this calibration remained constant. The zero of both strain gauge and mercury manometer for systemic pressure recording were set to the same approximate heart level before each experiment.

A note on catheter patency. Continuous care was necessary to ensure that the pial cannulae did not become blocked. The following points were of special importance:

The gauge and catheter system were filled with a dilute heparin solution (2 I.U./ml.). A three-way tap system, for aspiration and injection of the catheter excluding the gauge, proved unacceptably prone to leaks, and checking of the patency of the catheter was best achieved by close observation of the catheter as it emerged from the vessel, where to and

fro pulsation of blood was readily visible, together with the continued presence of a good pulse on the slow recorder trace. Between each observation, release of the filling catheter of the strain gauge allowed prompt backflow along the pial catheter which could then be gently filled again through the gauge. Blockage of the catheter, usually by angling of the tip against the vessel wall, occasionally by clotting, was detectable by a disappearance of the pulse, and of the oscillating saline/blood interface near the catheter tip. The catheters were treated with a silicone preparation (Repelcote: Hopkin and Williams, Ltd.) between experiments.

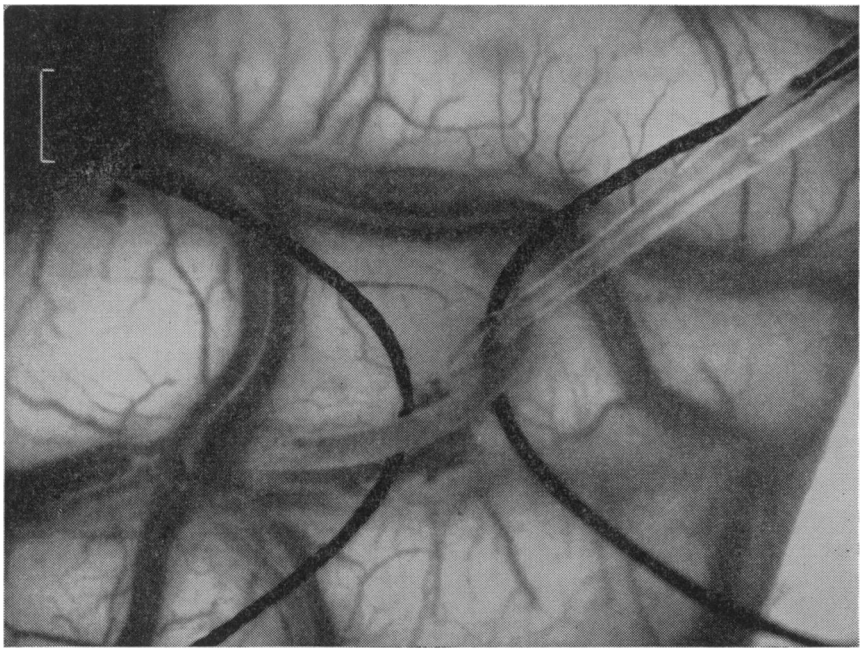

Fig. 1. Photograph of the cortical surface of a macaque brain. Threads have been passed beneath a leptomeningeal artery. The catheter is shown lying beside the vessel. The bracket represents 1 mm.

A note on preparation of the recordings. The use of two separate recording systems created several problems in illustration. The single-channel industrial constant speed recorder (Leeds and Northrup, Type 400), employed because of its wide pen excursion, had no time marker. The constant speed of this recorder was measured before and several times during each experiment against a stop-watch. No variation in the speed of this recorder was evident over several years use.

The speed of the kymograph and recorder being different, the slow recording was reduced photographically by the factor necessary to bring the 1/2 min intervals on the slow recorder chart paper to the same scale as the 1/2 min kymograph time marker. The kymograph and reduced slow recorder records for the same event were then lined up by the use of the event marks on each. In the course of the photographic reduction, the red on white slow recorder chart was reversed, for aesthetic reasons, to white on black. When both proximal and distal facing cannulae were inserted in the same middle cerebral branch, the pressure record from the second catheter, gauge and slow recorder was prepared in the same way.

At the end of each experiment, the occluded vessels were dissected after formalin fixation to confirm the details of any occlusion carried out.

RESULTS

Relation of pial arterial pressure to systemic arterial pressure

In both dogs and monkeys the blood pressure recorded from a parietal branch of the middle cerebral artery was lower than that in the femoral artery. In twelve dogs, under chloralose anaesthesia, the mean cerebral arterial pressure was between 88 and 95 % of mean femoral pressure (mean 90·1 S.D. ± 2·1). Under thiopentone the femoral blood pressure was lower than under chloralose anaesthesia, pulse pressure in the pial vessels was less, and the differences between middle cerebral and femoral pressures were the greatest observed, cerebral arterial pressure being 80, 82 and 82 % of femoral pressure in these three animals. In the six monkeys, the vessel used for cannulation was larger than in dogs, but the cerebral blood pressure was also between 80 and 90 % of the pressure in the femoral artery (mean 87·0: S.D. ± 4·0).

Occlusion of the main vessels in the neck

The carotid arteries. Occlusion of the ipsilateral common carotid artery caused a fall in the cerebral arterial pressure which was greater in the monkey than in the dog. In dogs there was a sharp drop with a variable recovery within ½ min to a level which then remained constant or rose slightly until the vessel was released. The extent of the initial fall varied considerably from animal to animal.

The more stable record which was rapidly obtained after this partial recovery, assessed in a group of eleven animals as a whole (38 observations), was between 80 and 95 % of the original cerebral arterial pressure (mean 90·1: S.D. ± 3·9). The fall obtained under thiopentone anaesthesia was greater than with chloralose anaesthesia. Thus, the residual pressure in ten observations in three animals under thiopentone anaesthesia was between 80 and 88 % (mean 85·3: S.D. ± 2·6). In twenty-eight observations in eight animals under chloralose anaesthesia, the residual pressure after ipsilateral common carotid occlusion ranged from 88 to 95 % of the original pressure (mean 94·0: S.D. ± 3·6). A comparison of these two groups by variance analysis using the F test by 't' test with common variance showed that they were significantly different ($P < 0{\cdot}005$).

Since, in monkeys, prolonged barbiturate anaesthesia resulted in a gradual fall in arterial pressure, the occlusion experiments in this species were performed only with chloralose anaesthesia. Occlusion of the ipsilateral common carotid artery resulted in a larger fall in middle cerebral

arterial pressure than in dogs, and there was usually no partial recovery during the period of occlusion (Fig. 2*c*). Even when the occlusion was maintained for as long as 5 min, little or no recovery occurred. The mean cerebral blood pressure after occlusion of the common carotid artery in twenty-eight observations in six monkeys varied between 75 and 85 % of its initial value (mean 79·6: S.D. ± 4·3).

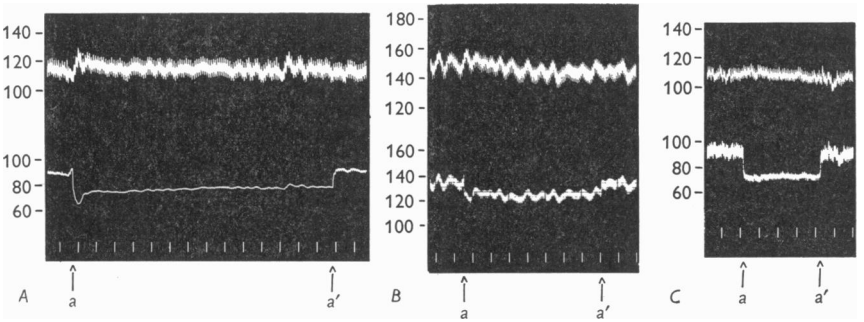

Fig. 2. The effects of occlusion of the common carotid artery on arterial pressure in the middle cerebral field. Records from above down: pressure in mm Hg in femoral artery, in middle cerebral artery, and time in periods of 30 sec. *A* and *B* are from dog experiments; *A*, thiopentone anaesthesia, *B*, chloralose. *C*, a macaque experiment, chloralose anaesthesia. In each case, the common carotid artery was occluded at *a* and released at *a′*.

Occlusion of the internal and external carotid arteries

In dogs, occlusion of the external carotid artery produced a result indistinguishable from occlusion of the common carotid, while occlusion of the internal carotid artery had no effect—as illustrated in Fig. 3*A*.

In the macaque, while occlusion of the external carotid artery had no influence on the cerebral arterial pressure, occlusion of the internal carotid artery produced an appreciable fall (Fig. 3*B*). This fall, however, was invariably less than that produced by occlusion of the common carotid artery, the pressure level after internal carotid occlusion in twenty observations in six animals remaining between 82 and 94 % of the pre-occlusion value (mean 86·2: S.D. ± 3·4). These results were compared with those obtained on the same animals after common carotid occlusion by *t* test using paired comparisons ($P < 0{\cdot}001$). These lesser pressure changes might be explained by some contribution from the external carotid artery to the cerebral circulation, although the absence of any pressure change when the external carotid was occluded alone makes this unlikely. This explanation is rebutted more conclusively, however, by the observations illustrated in Fig. 4. In this experiment, occlusion of the internal carotid artery at *a* produced a fall in cerebral arterial pressure, while the addition of common carotid occlusion at *b* did not increase this fall, showing that no

contribution to the cerebral arterial pressure was made from the external carotid artery. When the clamp on the internal carotid artery was then removed at a', there was a further sharp fall in cerebral arterial pressure, and a further reduction of pulse pressure, to levels such as were seen in this animal with common carotid occlusion. The external carotid artery was finally occluded at c and cerebral arterial pressure rose to a level closely similar to that seen with internal carotid occlusion alone. Subsequent

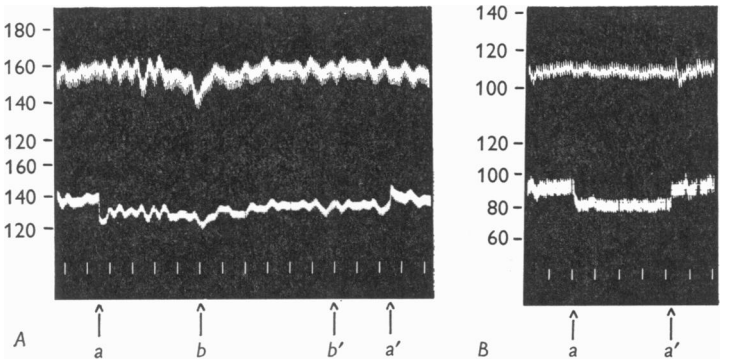

Fig. 3. *A*. Femoral arterial (above) and cerebral arterial pressure (below) in a dog, chloralose anaesthesia. Between the arrows a and a', the ipsilateral common carotid artery was occluded. Between the arrows b and b', the ipsilateral internal carotid artery was occluded. *B*. Femoral arterial (above) and cerebral arterial pressure (below) in a macaque, chloralose anaesthesia. The ipsilateral internal carotid artery was occluded at a and released at a'. Scales in mm Hg. Time marker intervals, 30 sec.

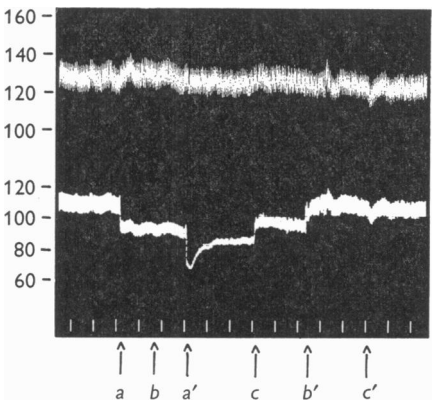

Fig. 4. Femoral arterial (above) and cerebral arterial pressure (below) in a macaque, chloralose anaesthesia. Between the arrows a and a' the ipsilateral internal carotid artery was occluded. Between the arrows b and b' the ipsilateral common carotid artery was occluded, and between the arrows c and c' the ipsilateral external carotid artery was occluded. Scales in mm Hg. Time marker intervals, 30 sec.

release of the common carotid artery at *b'* restored the normal level, but the additional release of the external carotid at *c'* was without effect. Since this pattern of pressure change was seen in all six animals in the present series, it seems likely that in the macaque, after common carotid occlusion, blood flows from the internal to the external carotid artery at the carotid bifurcation, so that the intracranial circulation bleeds in effect, into the extracranial. The fall in cerebral arterial mean and pulse pressure is, therefore, greater with occlusion of the common than of the internal carotid artery.

Occlusion of the contralateral common carotid artery

The effect of occlusion of the contralateral common carotid artery also differed in the two species. In the dog, there was little or no effect on middle cerebral arterial pressure. A fall of 3 mm Hg in mean pressure was the maximum seen in any experiment. In the macaque, occlusion of the contralateral common carotid invariably produced a fall, less than that produced by occlusion of the ipsilateral common carotid except in one of four animals. Residual cerebral arterial pressure remained between 83 and 92 % in thirteen observations in four animals (mean 86·9: S.D. ± 5·3). These observations were compared with the results of ipsilateral common carotid occlusion in the same four animals by *t* test using paired comparisons. There was a doubtfully significant difference ($P < 0{\cdot}05$).

Bilateral carotid occlusion

The effect of bilateral carotid occlusion in the two species illustrated the greater importance of the carotid supply to the forebrain in the macaque. In both species, the added fall in arterial pressure in the middle cerebral field which occurred when the second carotid artery was occluded was greater than that produced when this vessel was occluded singly. Figure 5*A* shows such an experiment on a dog. The pressure remaining after occlusion of both carotid arteries was between 75 and 89 % of the original observation in twenty-seven observations in nine animals (mean 82·9: S.D. ± 4·7). In eight of these animals, the results of ipsilateral common carotid occlusion alone was available for comparison of data by *t* test using paired comparisons. There was a significant difference from unilateral carotid occlusion in the eight animals ($P < 0{\cdot}001$).

Figure 5*B* illustrates a similar experiment in a macaque. Occlusion of the second (ipsilateral) carotid artery produced a precipitous fall in cerebral arterial pressure to 42 % of the original level with prompt recovery when the occlusions were released. In the systemic pressure recording illustrated there was a gradual elevation of blood pressure on occlusion of the second carotid artery, with a fall when this vessel was released, although both

carotid sinus nerves had been carefully cut. This effect has been described previously in dogs (Bouckaert & Heymans, 1935) and in rabbits (Chungcharoen, Daly, Neil & Schweitzer, 1952) and was attributed by them to the mechanical effect of reduction in capacity in the peripheral vascular bed with occlusion of two large vessels. In the present experiments such an effect was not seen in dogs, but occurred in each instance in macaques. The possibility that the effect might be due to baroreceptors in the carotid field other than the carotid sinus cannot be entirely excluded, although the application of a bulldog clip to the common carotid artery just below the bifurcation, the position employed in the present experiments, should not activate receptors in the common carotid artery such as those described by Green (1953) in the cat, which lay at several sites in the common carotid artery some distance below the common carotid bifurcation.

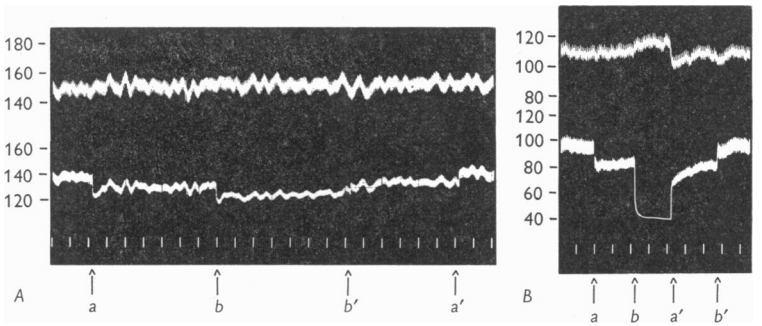

Fig. 5. *A*. Femoral arterial (above) and cerebral arterial pressure (below) in a dog, chloralose anaesthesia. Between the arrows *a* and *a′* the ipsilateral common carotid artery was occluded. Between the arrows *b* and *b′* the contralateral common carotid artery was occluded. *B*. Femoral arterial (above) and cerebral arterial pressure (below) in a macaque. Between the arrows *a* and *a′* the contralateral common carotid artery was occluded. Scales in mm Hg. Time marker intervals, 30 sec.

The level of the middle cerebral arterial pressure recorded during twenty-five bilateral carotid occlusions in six macaques was between 33 and 52 % of pre-occlusion values (mean 42·3 : S.D. ± 6·0) and was repeatedly the same in any given animal.

Occlusion of the vertebral arteries in the neck

The contribution of the vertebral arteries to the blood supply of the brain above the tentorium differs in dogs and monkeys. This is illustrated by the effect of occlusion of these vessels on the arterial pressure in the middle cerebral field. In dogs, while occlusion of one or other vertebral artery was without perceptible effect, occlusion of both vertebral arteries together produced a sharp fall in pressure only slightly less than that pro-

duced by occlusion of the ipsilateral common carotid artery, with attainment within ½ min of a stable level, some 90–95 % of pre-occlusion values in twenty-six observations in eight animals (mean 92·8: S.D. ± 1·8) (see Fig. 6). In the macaque, on the other hand, occlusion of both vertebral arteries was without effect on the arterial pressure in the middle cerebral field (see Fig. 7). Experiments reported elsewhere (Symon, Ishikawa & Meyer, 1963) have, however, shown that occlusion of both vertebral arteries in the macaque reduces the cerebral arterial pressure recorded from a small branch of the posterior cerebral artery.

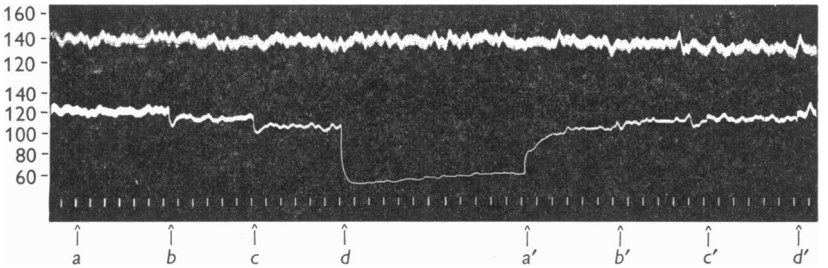

Fig. 6. Femoral arterial (above) and cerebral arterial pressure (below) in a dog, chloralose anaesthesia. At the arrows *a* and *b*, the contralateral and ipsilateral vertebral arteries were occluded. At the arrows *c* and *d* the contralateral and ipsilateral common carotid arteries were occluded. The vessels were released in the same order at *a′*, *b′*, *c′* and *d′*. Scales in mm Hg. Time marker intervals, 30 sec.

Simultaneous occlusion of vertebral and carotid vessels

Occlusion of both carotid and both vertebral arteries produced a depression of cerebral arterial pressure which differed considerably in extent in the two species. An experiment in the dog is shown in Fig. 6, where after occlusion of the four neck vessels in series, the cerebral arterial pressure fell to 40 % of the initial pressure, gradually rising to 46 % of the initial pressure over the next 6 min, without change in the systemic arterial pressure or alteration in respiration to suggest anoxia of the vital centres. The final level of cerebral arterial pressure when the four neck vessels were occluded in twenty-five observations in eight dogs lay between 35 and 50 % of normal (mean 45·0: S.D. ± 4·3), with a slight but variable rise over the next few minutes until the release of the occlusion. It is clear that in this species collateral channels from the muscular vessels of the neck are sufficient to maintain the vital centres even after flow in the main arteries in the neck has been interrupted.

In the macaque, occlusion of the four neck vessels had a much greater effect, residual cerebral arterial pressure falling to between 10 and 14 % of pre-occlusion values in twenty observations in six animals (mean 11·3: S.D. ± 1·6). Such an experiment is shown in Fig. 7. The level of cerebral

arterial pressure after occlusion of all four vessels in this experiment was 10 mm Hg or 11 % of pre-occlusion mean pressure. Simultaneously the systemic arterial pressure rose from 100 mm Hg within ½ min, a response to medullary ischaemia which was at once terminated by removal of one of the arterial clamps at *a'*—in this instance the contralateral vertebral artery, yet the arterial pressure in the middle cerebral field was only 23 % of normal.

The effect of occlusion of the middle cerebral artery

In both species, occlusion of the middle cerebral artery produced a sudden fall in the arterial pressure recorded from an ascending parietal branch of that vessel. In the nine dogs in which the middle cerebral artery

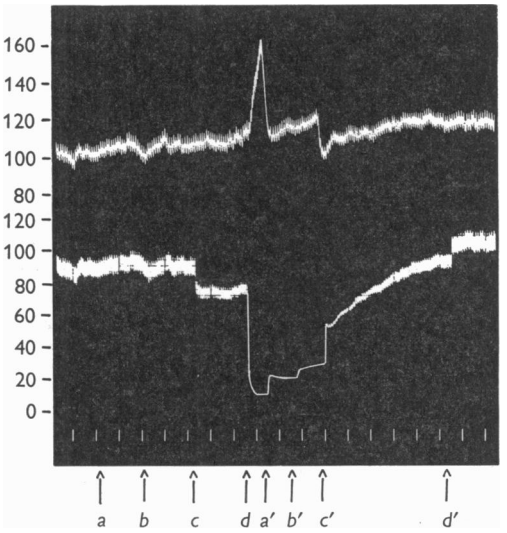

Fig. 7. Femoral arterial (above) and cerebral arterial pressure (below) in a macaque, chloralose anaesthesia. At the arrows *a* and *b* the contralateral and ipsilateral vertebral arteries were occluded. At the arrows *c* and *d* the contralateral and ipsilateral carotid arteries were occluded. The vessels were released in the same order at *a'*, *b'*, *c'* and *d'*. Scales in mm Hg. Time marker intervals, 30 sec.

was occluded, the minimum level recorded was between 15 and 30 mm Hg or 18–30 % of the initial pressure (mean 24·3: S.D. ± 3·8) and there was a variable recovery within the first 5 min after occlusion to between 25 and 40 % of pre-occlusion level. The common type of effect seen in seven dogs is shown in Fig. 8*A*. On occlusion of the middle cerebral artery at *a*, pressure in the middle cerebral field fell from a mean level of 100 mm Hg to one of 23 mm Hg. Five minutes after occlusion, pressure had risen to 30 mm Hg. Less common (two dogs) was a rather sharper initial recovery in the first few minutes with the appearance of a slight pulse pressure in the

pial vessels. Later there occurred in all experiments a gradual recovery, which varied from animal to animal. Measurements were made up to 1 hr after occlusion in seven animals, when a pressure of between 30 and 50 % of pre-occlusion level had been reached (mean 39·6: S.D. ± 6·6).

In the six macaques, there was a similar rapid fall in pressure in the cannulated ascending parietal branch when the middle cerebral artery was occluded, the minimum level reached being between 20 and 27 mm Hg or 20–30 % of the initial pressure (mean 25·2: S.D. ± 3·9), but there was little or no recovery thereafter, as shown in Fig. 8*B*. Occlusion of the middle cerebral artery at *a* resulted in a sharp fall in pressure to 30 % of pre-occlusion value. In this experiment there was no apparent recovery either during the next few minutes or later, and in no experiment did recovery amount to more than 2–3 mm Hg.

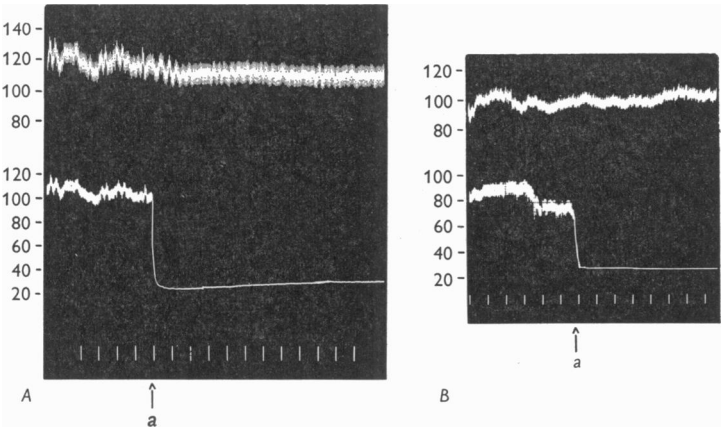

Fig. 8. *A*. Femoral arterial (above) and cerebral arterial pressure (below) in a dog, chloralose anaesthesia. At the arrow *a* the middle cerebral artery was occluded. *B*. Femoral arterial (above) and cerebral arterial pressure (below) in a macaque, chloralose anaesthesia. At the arrow *a* the middle cerebral artery was occluded. Scales in mm Hg. Time marker intervals 30 sec.

The level of arterial pressure recorded from the proximal end of a branch of the middle cerebral artery after occlusion of the main trunk is dependent upon the available collateral vessels; it can, therefore, be regarded as some measure of collateral function. This residual pressure was further reduced, in both species, by occlusion of vessels in the neck, the pattern of reduction then following that previously seen with the middle cerebral artery intact.

In three dogs and two macaques before occlusion of the middle cerebral artery both the proximal and distal ends of a convenient ascending parietal vessel were cannulated in order to record blood pressure from both directions. The distal pressure record was then a measure of the collateral function available to a small area of the middle cerebral field, the distri-

bution of the divided ascending parietal vessel. In both species this pressure was unexpectedly high. In the dogs it was 70, 76 and 85 % of the proximal pressure and 65 and 70 % in the two macaques. In the dogs, there was an appreciable pulse pressure in the distal record, and the collateral flow between the branches of the middle cerebral artery was so great that saline injected retrograde into the proximal cannula was seen rejoining the vessel by side branches distal to the cannulae. In the macaques, the distal recording was more 'damped' compared with the proximal record.

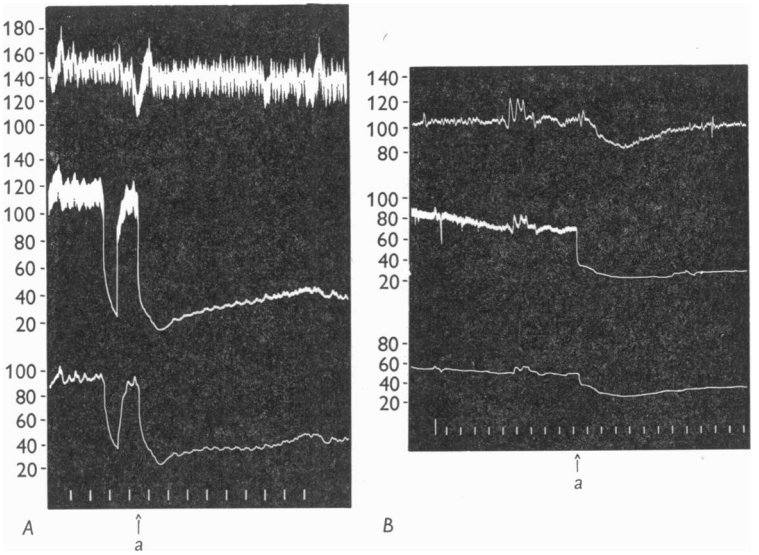

Fig. 9. *A*. Blood pressure records from a dog, chloralose anaesthesia. The upper record is femoral blood pressure. The middle and lower records are from the proximal and distal ends respectively of an ascending parietal branch of the middle cerebral artery. At the arrow *a* the middle cerebral artery was occluded. *B*. Blood pressure records from a macaque, chloralose anaesthesia. The upper record is femoral blood pressure. The middle and lower records are from the proximal and distal ends respectively of an ascending parietal branch of the middle cerebral artery. At the arrow *a* the middle cerebral artery was occluded. Scales in mm Hg. Time marker intervals, 30 sec.

The distal pressure in both dogs and macaques depended in considerable measure upon the integrity of the main middle cerebral trunk. When this vessel was occluded, there were approximately parallel changes in the pressure recorded from proximal and distal cannulae, as illustrated in Fig. 9*A* and *B*.

Figure 9*A* is from an experiment in a dog. There is evident close similarity between the proximal and the distal record. The middle cerebral

artery was occluded at *a*. The sharp transient fall preceding occlusion occurred when the artery was being mobilized and was temporarily occluded by a blunt hook.

A similar experiment in the macaques is illustrated in Fig. 9*B*. The occlusion at *a* resulted in a sharp fall in the proximal record paralleled by a similar though smaller fall in the distal record.

The results of these experiments indicate that in both the dogs and macaques, part of the collateral pressure in the distribution of a small branch in the middle cerebral artery arose from the main middle cerebral artery through contiguous branches. Thus when the main vessel was occluded, a further fall in pressure occurred in the field already isolated from the main middle cerebral flow.

DISCUSSION

These experiments demonstrate considerable difference between the dog and monkey in the effects upon cerebral arterial pressure of occlusion of various neck and cerebral vessels.

The changes in middle cerebral arterial pressure with occlusion of external or internal carotid arteries in dogs are similar to those described by Chungcharoen *et al.* (1952) in the distal end of the divided common carotid artery. They reflect the importance in the cerebral arterial supply of this species of the arteria anastomotica, a large vessel running from the internal maxillary artery to join the intracranial part of the internal carotid artery in the cavernous sinus, which has been extensively described (Bouckaert & Heymans, 1935; Chungcharoen *et al.*, 1952). It is clear that, in the dog, alterations in pressure in the extracranial circulation may considerably influence intracranial haemodynamics, a factor which must continually be borne in mind in investigations where cerebral blood flow measurements are made in this species by assessing the distribution in or dispersal from cortex of material injected into the carotid artery in the neck.

The results of carotid occlusion in the macaque confirm that the external carotid artery plays no detectable role in the maintenance of normal intracranial blood pressure. It is further evident that in this species immediately after common carotid occlusion, the normal direction of flow at the carotid bifurcation is from the internal to the external carotid arteries. Similar findings were reported by Hardesty, Roberts, Toole & Royster (1960) using an electromagnetic flowmeter in 50 % of human cases.

After common carotid occlusion in the dog, the immediate fall in cerebral arterial pressure was succeeded by a partial recovery in 15–45 sec. It seems reasonable to attribute this recovery in cerebral arterial pressure to dilatation of collateral channels under the influence of decreased intra-

luminal pressure, the effect originally described by Bayliss in 1902, provided that no change in systemic blood pressure occurs during this time. Schwartz, Harris & Mahoney (1961), however, have described a reduction in blood flow in the peripheral distribution of an artery during the mobilization of the vessel, as evidenced by a reduction in muscle oxygen tension, and have attributed it to reflex vasospasm, since it was abolished by sympathectomy or by procaine or papaverine applied locally to the vessel. Such changes were unaccompanied by alterations in systemic blood pressure. In the present experiments mere handling of the carotid vessels after denervation of the carotid sinus did not produce any detectable change in cerebral arterial pressure apart from systemic pressure fluctuations. While it is possible, therefore, that the resolution of transient reflex vasospasm may play a part in the partial restoration of cerebral arterial pressure soon after carotid occlusion, it seems more likely that this is the result of collateral dilatation, provided that no alteration in systemic blood pressure occurs.

The early partial recovery in cerebral arterial pressure invariably seen in dogs after carotid occlusion in the present study was rarely seen in the macaque, nor is it apparent in the recordings of Bakay & Sweet (1952) in human cases. This species difference may depend upon the fact that, in the dog, the cerebral arterial blood supply is conveyed by external carotid vessels almost until the circle of Willis, whereas in the macaque and man it is predominantly internal carotid in route. The difference may be explained solely on anatomical grounds, or it may reflect a greater functional capacity for collateral dilatation within the external carotid circulation. The number of collateral channels available to contribute to the occluded cerebral blood supply is greater if all the branches of the external artery between the carotid sinus and the arteria anastomotica may play a part, than if the only vessels available are those of the circle of Willis itself.

The effect of occlusion of the carotid and vertebral arteries in the neck also differed significantly in the two species, indicating the relatively greater influence of the vertebro-basilar system in the maintenance of cerebral arterial pressure in the forebrain of the dog, and the greater predominance of the carotid vessels in the macaque. A further species difference was evident after occlusion of both carotid and both vertebral arteries. In dogs, the cerebral arterial pressure remained above 40 mm Hg, and there was no rise in systemic blood pressure. In the macaque, on the other hand, occlusion of both vertebral and carotid arteries together produced a fall in cerebral arterial pressure to below 20 mm Hg with a prompt rise in systemic blood pressure. Since in those animals both carotid sinuses had been completely denervated, so that no appreciable rise in blood pressure followed bilateral carotid occlusion, the hypertensive response to

the occlusion of all four vessels must have been due to medullary ischaemia. The release of one vertebral artery resulted in a rise in cerebral arterial pressure to between 20 and 30 mm Hg, with a prompt subsidence of the systemic hypertension. It would appear, therefore, that the arterial pressure threshold of the medullary ischaemic response was between 20 and 30 mm Hg, under the conditions of the present experiments. This interpretation is open to the objection that the arterial pressure in the vessels of the brain stem, the relevant factor in the development of the medullary ischaemic response, may have been appreciably greater than the cortical arterial pressure both during occlusion of the neck vessels and after release of one vertebral artery. Thus, Sagawa, Ross & Guyton (1961) estimated the critical level for the medullary ischaemic response in dogs by perfusion of the isolated head at constant pressure, as in the region of 50 mm Hg arterial perfusion pressure, which they suggested might correspond to a cerebral arterial pressure of 40 mm Hg. At these low levels of blood pressure, however, particularly in a 'separated head' preparation such as they employed, the pressure difference between the small vessels in the medulla and the input perfusion pressure is likely to be greater than 10 mm Hg so that the threshold for the medullary ischaemic response in the two species may be at similar levels, in the region of 25–30 mm Hg.

The main anastomotic vessels which maintain the cerebral arterial pressure after ligation of both carotid and vertebral vessels have been shown, in the dog, to be between branches of the thyrocervical and ascending cervical branches of the subclavian artery, and muscular and descending branches of the vertebral and posterior auricular arteries (Cooper, 1836; Andreyev, 1935). Similar anastomoses have been described in the macaque (Donald & White, 1961).

The present finding of an appreciable arterial pressure distal to occlusion of the middle cerebral artery in both dogs and monkeys is in keeping with the presence of anastomoses in the leptomeninges between the peripheral branches of the middle cerebral artery and branches of neighbouring vessels. These anastomoses have been demonstrated anatomically many times (Heubner, 1872; Beevor, 1907; Vander Eecken & Adams, 1953) and function within a few moments of vascular occlusion in both the dog and macaque (Symon, 1960, 1961). In the present experiments, both species showed an immediate fall in arterial pressure within the middle cerebral field on middle cerebral occlusion to similar levels, between 18 and 30 mm Hg, but in dogs there was frequently an elevation of this pressure within 2 or 3 min, and several dogs showed a restoration of pulse distal to the occlusion. These changes were not seen in macaques, suggesting that although the arterial pressure levels were little different in the two species, collateral circulation in the leptomeninges was greater in the dog than in the macaque. In both

species, subsequent occlusion of the neck vessels produced further reduction in the residual cerebral arterial pressure indicating that this pressure was not merely a static pressure within a closed system, but was maintained by vessels communicating with both carotid and vertebral systems.

In the present experiments, arterial pressure recorded from the distal end of a divided middle cerebral arterial branch was some 60–85 % of that recorded from the proximal end of the same vessel, the lower range of values being obtained in macaques. In both species, with subsequent occlusion of the main middle cerebral artery, pressure in both ends of the divided branch fell sharply to reach a common level, indicating considerable collateral flow into the territory of the divided leptomeningeal artery from the neighbouring branches of the middle cerebral artery. Despite Vander Eecken's opinion (1959) that anastomoses between the various branches of any one cerebral artery such as have been demonstrated in dogs and man (Schmidt, 1955*a*, *b*) are much less common than anastomoses between the branches of contiguous cerebral arterial fields, it is clear that obstruction of a small middle cerebral branch in the leptomeninges causes a less profound fall in pressure in the distribution of this branch than does obstruction of the middle cerebral artery itself. These observations apply only to the pial vessels of a size between 300 and 600 μ in the species studied, for it has been shown by Penry & Netsky (1960) that the small cortical perforating arteries within the middle cerebral distribution are functionally end-arteries.

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