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THE ORIGIN OF THE HYPERGLYCAEMIC RESPONSE TO INTRACISTERNAL ADRENALINE IN THE CAT: THE SITE OF SYSTEMIC ABSORPTION AND OF CENTRAL ACTION OF ADRENALINE FROM THE SUBARACHNOID SPACE

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An intracisternal injection of adrenaline in the cat produces a pronounced hyperglycaemia which has been attributed by Leimdorfer, Arana & Hack (1947) to a central action of the amine. However, it has recently been shown that this hyperglycaemia is largely attributable to peripheral action following absorption of the adrenaline into the blood stream, although a central component, mediated by the splanchnic nerves, does contribute to the resultant hyperglycaemia (Sproull, 1963).

The present experiments, carried out to determine the site or sites of the systemic absorption and of the central action of intracisternally injected adrenaline, have shown that the main sites on and through which adrenaline acts from the subarachnoid space lie in the tuberal region on the ventral surface of the brain.

METHODS

Cats of 2–4 kg body weight were anaesthetized with amytal sodium, 170–200 mg, injected intraperitoneally, and tracheotomy was performed. For the withdrawal of blood samples a vinyl cannula, 0·90 mm external diameter × 0·45 mm bore, was passed into the inferior vena cava through the saphenous vein.

Direct introduction of adrenaline into the cisterna magna

The cisterna was exposed by removing the muscles over the atlanto-occipital membrane and then incising the dura and arachnoid. To retain the cerebrospinal fluid, the cats were placed on the belly, in a head-down ('gargoyle') position, with full flexion of the atlanto-occipital joint, which was elevated to make the cisterna magna become the highest point in the subarachnoid space. The adrenaline, in various doses, was dropped directly into the cisterna, after removal of some of the cerebrospinal fluid. In some experiments, in order to prevent ready access of the adrenaline to either the dorsal, lateral, or ventral surfaces of the medulla or the junction between the medulla and spinal cord, the area to be excluded from the adrenaline was covered with blood clot. After removing the surrounding cerebrospinal fluid, fresh blood immediately followed by thrombin (Parke, Davis & Co.) was applied to the area. An adherent clot instantly formed. The posterior cranial fossa was then refilled

with artificial cerebrospinal fluid. In other experiments, in order to establish whether the extraventricular choroid plexuses over the foramina of Luschka were necessary for the hyperglycaemic response to intracisternal adrenaline, the plexuses, after exposure of the cisterna magna, were removed through the fourth ventricle, either after splitting the vermis of the cerebellum or by simply removing the plexuses together with the cerebellum by suction. At the end of each experiment, 0·2 ml. of Evans blue solution was dropped into the cisterna magna, as the adrenaline had been, and the distribution of the dye on the surface of the brain was examined post-mortem.

Injection of adrenaline at other sites

The adrenaline, 25 μg in 0·05 ml., was injected at one of the following seven sites:

Third ventricle. After a frontoparietal craniotomy a vinyl cannula was passed under the genu of the corpus callosum, to perforate the lamina terminalis and so enter the ventricle. In Fig. 1*b* this route is indicated by the arrow *V*.

Fourth ventricle. The injection was made with a fine hypodermic needle, after exposure of the cisterna magna, through the membranous roof of the ventricle over the calamus scriptorius.

The subarachnoid space over the dorsal or lateral surface of the mid-brain. Through a parieto-occipital craniotomy the medial occipital cortex was removed on one side, to expose the tentorium of the cerebellum; a vinyl cannula was then passed, either in the mid line or laterally, over the rostral edge of the tentorium. This route is indicated in Fig. 1*b* by the arrow *MB*.

Interpeduncular fossa. The fossa, the position of which is shown in Fig. 1*a*, was cannulated through the mouth; in the basilar part of the occipital bone a hole was made, through which a vinyl cannula was inserted in the mid line into the subarachnoid space, to pass between the bifurcation of the basilar artery and the inferior petrosal sinus, and so into the fossa. This route is indicated by the arrow *I* in Fig. 1*b*.

Cisterna terminalis (ct in Fig. 1*a*). It was cannulated through the third ventricle; a 5–6 mm width of the parietal bone was removed on one side of the mid line, the membranes were opened, and the medial 2–3 mm of cerebral cortex was sucked away to expose the corpus callosum, which was split with a knife to open the third ventricle; the cannula, which for this purpose consisted of a 4 cm length of stainless-steel tube, of 1 mm diameter, tipped with a 5 mm length of hard polythene tube, was then passed in the mid line through the massa intermedia, at an angle of about 40° to the horizontal, until its tip was felt to make contact with the sphenoid bone. The cannula in position is shown in Fig. 1*b*.

The subdural space under the cisterna terminalis was cannulated like the cisterna, but the cannula was finally rotated with firm pressure through the arachnoid and into the subdural space.

The pontine subdural space was reached by the same route as the interpeduncular fossa, the cannula being passed between the dura and the arachnoid.

In all experiments the insertion of the cannula was completed before the first blood sample was taken, and the cats were placed in the following positions: When the interpeduncular fossa was cannulated, the cats were left in the operating position, on the back, with the head raised slightly; for injection into the fourth ventricle the 'gargoyle' position was adopted; and in the other instances, when the cannula passed through a calvarial craniotomy, the cats were left in the head-holder, in a prone, head-up, sphinx-like position. At the end of the experiments 0·05 ml. Evans blue solution was injected through the cannula, and the location of the tip of the cannula was confirmed post mortem.

Injection of adrenaline into the cisterna magna after hypophysectomy

Hypophysectomy was performed by the transbuccal route, the gland being removed by suction or with Hartmann's aural forceps. To control the often profuse venous haemorrhage

from the region of the posterior clinoid process, the empty pituitary fossa was packed with a dental cotton-wool ball, and finally the defect in the sphenoid bone was sealed with acrylic dental cement. The cat was then placed in the prone, head-up position for the subsequent intracisternal injection, which was made through a small mid-line incision in the skin over the atlanto-occipital joint. The success of the hypophysectomy was determined post mortem by examination of the fixed brain with a hand lens.

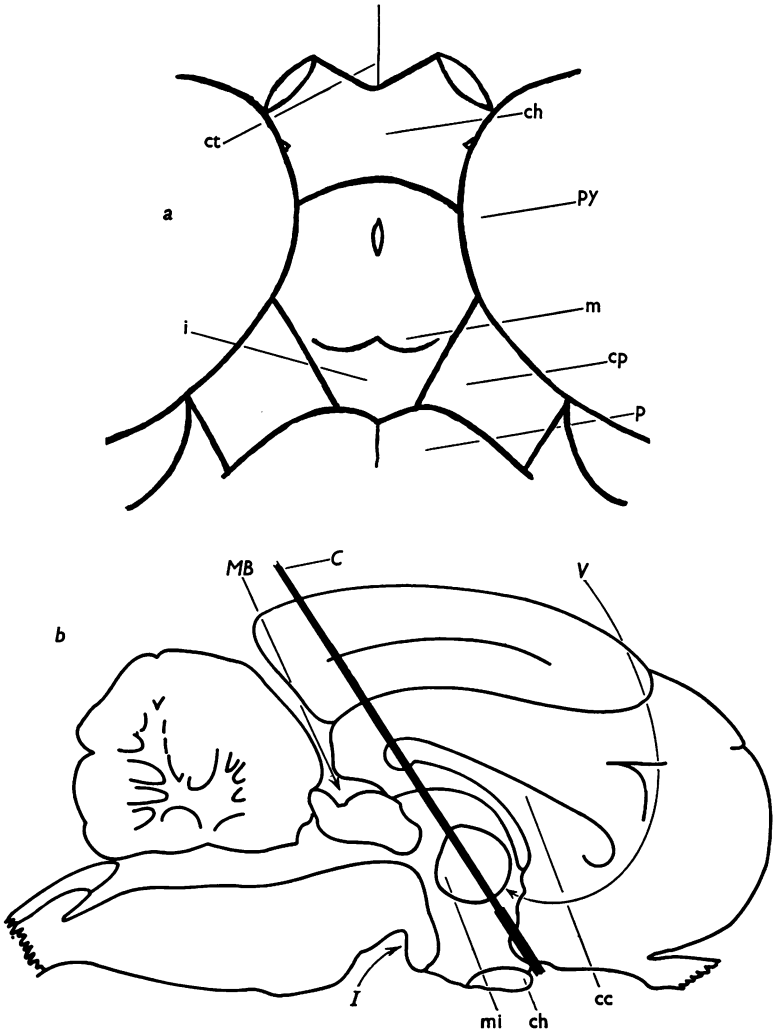

Fig. 1. *a*, Diagram of the ventral surface of the cat brain after removal of the hypophysis, showing the position of the interpeduncular fossa (i) and of the cisterna terminalis (ct). *b*, Mid-sagittal section of the cat brain with the cannula (*C*) in the cisterna terminalis. The arrows indicate the routes of the other cannulations: *V*, third ventricle; *MB*, mid-brain; *I*, interpeduncular fossa. The small letters indicate ch, optic chiasma; py, pyriform lobe; m, mamillary body; cp, cerebral peduncle; p, pons; cc, corpus callosum; mi, massa intermedia.

Drugs

The adrenaline used was the bitartrate, dissolved in artificial cerebrospinal fluid (Merlis, 1940): the doses are expressed in terms of the base.

The Evans blue solution was made up to 1 g/100 ml. artificial cerebrospinal fluid, and the volume used was always the same as that of the preceding dose of adrenaline.

Blood samples, for the estimation of blood glucose concentration, were taken at 20 min intervals for 140 min. Three samples were taken in each experiment before the adrenaline was given. Blood glucose concentration was determined by the specific glucose oxidase method of Huggett & Nixon (1957), and the procedure followed was the same as that described by Hasselblatt & Sproull (1961).

RESULTS

Opening the exposed dura and arachnoid had an effect on the blood glucose concentration, depending on the position of the cat's head. When the cat was held in a sphinx position, with the head in a nearly horizontal plane, opening of the membranes was followed by a progressive increase in blood glucose concentration, as shown in the experiment in Fig. 2.

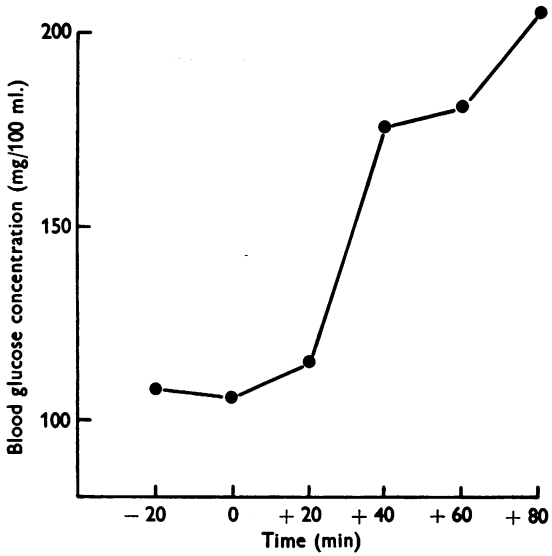

Fig. 2. The increase in blood glucose concentration of an anaesthetized cat held in the sphinx position. At zero time the dura and arachnoid were opened, with loss of cerebrospinal fluid.

On the other hand, when the cat was held in the gargoyle position, with the head flexed into a vertical plane and raised above the level of the body so that the cisterna magna was the highest part of the subarachnoid space, opening the membranes no longer affected the blood glucose concentration. This is shown by the results in the first line of Table 1. The difference

TABLE 1. The blood glucose concentrations of cats before and after the direct introduction of adrenaline into the exposed cisterna magna at zero time. For comparison, the results of Sproull (1963) for the injection at zero time of adrenaline into the cisterna magna are given in line 7*. In the experiments of the second to sixth lines the membranes were opened at −45 min. The figures in parentheses refer to the number of replications in sets with missing observations

Dose of adrenaline (μg)	No. of cats	Time (min)							
		−40	−20	0	+20	+40	+60	+80	+100
		Blood glucose concentration (mg/100 ml., mean ± S.D.)							
None	7	79 ± 17	83 ± 10	82 ± 8	84 ± 9	75 ± 11	88 ± 8	90 ± 10(4)	95 ± 8(4)
10	3	96 ± 9	101 ± 15	101 ± 11	121 ± 22	129 ± 18	141 ± 32	—	—
25	4	77 ± 9	82 ± 8	87·5 ± 7	112 ± 19	132 ± 19	144 ± 21	—	—
35	2	89·5 ± 3	94·5 ± 12	98 ± 7	153·5 ± 15	208 ± 74	222 ± 94	214 ± 82	—
50	3	95 ± 10	97 ± 12	102 ± 9	176 ± 37	232 ± 57	243 ± 65	245 ± 62	245 ± 73
100	7	94 ± 11	94 ± 10	94 ± 8	184 ± 46	219 ± 36	237 ± 42	238 ± 38	235 ± 33(6)
50*	6	87 ± 9	89 ± 10	88 ± 11	195 ± 15	221·5 ± 19	218·5 ± 12	215·5 ± 11	212·5 ± 6
100†	3	86 ± 1	86 ± 3	93 ± 7	209 ± 47	252 ± 32	266 ± 37	274 ± 40	281 ± 38
100‡	3	99 ± 4	94 ± 13	92 ± 13	142 ± 13	192 ± 11	227 ± 7	240 ± 20	250 ± 22

† Extraventricular choroid plexus removed. ‡ Cerebellum removed.

between the two positions is that in the gargoyle position the cerebrospinal fluid around the brain is retained, whereas in the sphinx position it is lost, so that the base of the brain may be resting on the vessels of the circle of Willis, which might account for the hyperglycaemia. In all subsequent experiments in which the cisterna magna was opened the cat was therefore held in the gargoyle position.

Direct introduction of adrenaline into the cisterna magna

The effects of several doses of adrenaline dropped into the cisterna magna are summarized in Table 1. With 10 or 25μg there was a slow, moderate increase in blood glucose concentration; with higher doses, increases to over 200 mg/100 ml. were obtained. The hyperglycaemia produced by 35–100 μg ultimately reached the same or an even higher level than those obtained in previous experiments on intracisternal injection of 50 μg adrenaline (Sproull, 1963), but developed somewhat more gradually. The distribution of Evans blue placed in the cisterna magna was the same as after its intracisternal injection: the dye spread down the upper cervical cord, around the pons and medulla, through the interpeduncular fossa to the parahypophysial region; no dye was seen on the cerebellar or cerebral cortices.

The seven experiments with 100 μg adrenaline summarized in line 6 of Table 1 include four in which certain regions of the brain stem were covered with blood clot. In one the spinal cord was surrounded with blood clot at its junction with the medulla. At the end of the experiment it was shown that Evans blue placed in the cisterna did not stain the surface of the upper cervical cord, so that access of adrenaline to this region was impeded. In the other experiments either the dorsal or both lateral surfaces of the medulla, or the ventral surfaces of the pons and medulla were covered with blood clot, and Evans blue placed in the cisterna at the end of the experiment did not stain the surface of the brain stem underneath the clot. Covering these various regions with blood clot did not modify the hyperglycaemic responses, which were not less than those obtained in the other three experiments. This suggested that ready access of the adrenaline to the cervical cord, to the posterior, lateral, or ventral surfaces of the medulla, or to the surface of the pons is not necessary for the hyperglycaemic response.

Table 1 also includes experiments in which the effect of 100 μg adrenaline was studied after removal of the extraventricular choroid plexuses over the foramina of Luschka or of the cerebellum. Removal of the choroid plexuses caused a slight enhancement of the response, possibly due to more rapid penetration of the adrenaline through the posterior cranial fossa. Removal of the cerebellum caused a slight reduction in the hyperglycaemic

response, probably due to the greater dilution of the adrenaline resulting from replacement of the cerebellum by an equivalent volume of cerebrospinal fluid.

Injection of adrenaline at other sites

To locate the sites which have to be reached by intracisternally injected adrenaline in order to produce its hyperglycaemic effect, a dose of 25 μg, which is almost a threshold dose when it is dropped into the exposed cisterna magna, was applied to various regions. The results are summarized in Table 2.

On injection into the third ventricle the adrenaline was ineffective; on injection into the fourth ventricle it produced a delayed response, but one which was greater than that obtained when 25 μg was dropped into the cisterna magna. These results show that the adrenaline does not act from the ventricular spaces, but must pass into the subarachnoid space; and further that the regions on which it is effective are reached more easily through the foramina of Luschka than from the cisterna magna, i.e. the regions must be cephalic to the foramina. These regions do not lie on or near the dorsal or lateral surfaces of the mid-brain, since the hyperglycaemic response was less on injection of 25 μg adrenaline into the subarachnoid space over the colliculi or at the side of the mid-brain than on its injection into the fourth ventricle. These conclusions, which suggest that the effective sites lie on the ventral surface of the brain rostral to the foramina of Luschka, are supported by the distribution of dye injected at the end of the experiments. After injection into the fourth ventricle the dye passed through the foramina of Luschka, ventrally into the cisterna pontis, and through the interpeduncular fossa to the tuberal region; injected over the colliculi or the lateral aspects of the mid-brain, the dye did not diffuse ventrally, but around the dorso-lateral mid-brain and the pineal region.

When applied to the ventral surface of the brain the effect of the adrenaline was different on injection into the interpeduncular fossa or into the cisterna terminalis. As is shown in Table 2 and Fig. 3, the injection of 25 μg into the fossa produced a hyperglycaemic response as great as after double this dose by intracisternal injection; dye injected into the fossa spread rostrally to around the tuber cinereum and then centrifugally along the main cerebral arteries. Injection of 25 μg adrenaline into the cisterna terminalis was ineffective, and injected dye spread along the paths of the anterior and middle cerebral arteries, none appearing on the ventral surface of the brain caudal to the chiasma.

Thus only a small region on the ventral surface of the brain, bounded caudally by the interpeduncular fossa and rostrally by the optic chiasma, has apparently to be reached by intracisternally injected adrenaline to

TABLE 2. The blood glucose concentrations of cats before and after the application at zero time of 25 μg adrenaline to various sites in the ventricular system, subarachnoid, and subdural spaces

Site of application	No. of cats	Time (min) −40	−20	0	+20	+40	+60	+80	+100
		Blood glucose concentration (mg/100 ml., mean ± S.D.)							
Third ventricle	4	78 ± 3	81 ± 3	78·5 ± 4	91 ± 11	94 ± 10	97 ± 8	95 ± 8	97·5 ± 9
Fourth ventricle	5	88 ± 9	86 ± 11	91 ± 12	108 ± 23	153 ± 21	189 ± 32	208 ± 40	216 ± 37
Subarachnoid space: lateral and dorsal mid-brain	9	90·5 ± 9	90 ± 9	94 ± 13	125 ± 18	147 ± 23	161 ± 26	165 ± 29	170 ± 31
Interpeduncular fossa	2	88·5 ± 3	84 ± 2	84 ± 2	189·5 ± 3	221·5 ± 54	213 ± 57	199·5 ± 52	182·5 ± 38
Cisterna terminalis	8	81 ± 10	80 ± 11	79 ± 10	84 ± 9	88 ± 11	91·5 ± 11	100 ± 13	105 ± 12
Through cisterna terminalis into subdural space	6	81 ± 9	80 ± 9	80 ± 8	173·5 ± 27	179 ± 39	178·5 ± 32	172 ± 25	172 ± 21
Pontine subdural space	5	93 ± 12	95 ± 12	95·5 ± 13	101 ± 12	103 ± 15	106 ± 16	107 ± 20	108 ± 18

elicit the full hyperglycaemic response. The region contains the interpeduncular fossa, mammillary bodies, tuber cinereum and pituitary stalk.

Absorption of adrenaline through the pituitary was suggested by experiments in which the adrenaline was injected into the subdural space. The strip of the pars distalis which lies between the arachnoid and the diaphragma sellae (Schwartz, 1936) is reached by an injection into the subdural space underlying the cisterna terminalis, i.e. in the triangular area

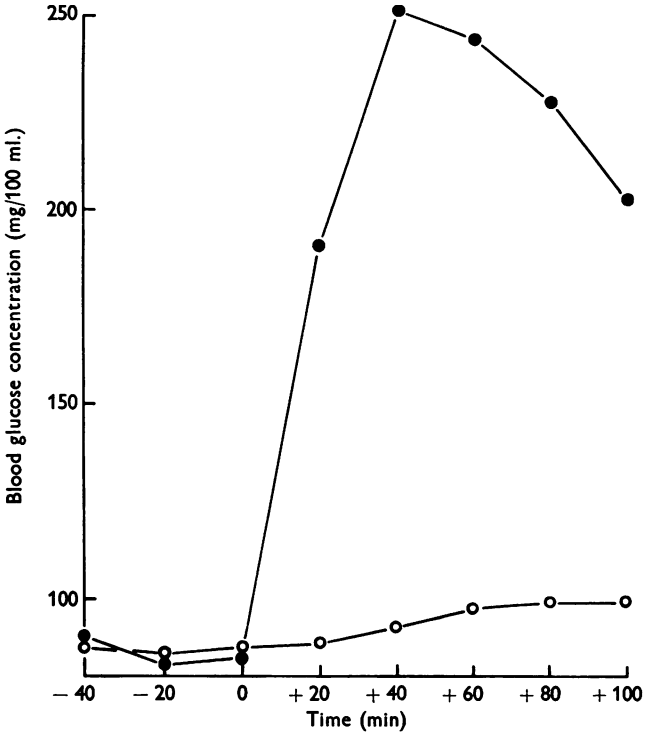

Fig. 3. Effects in anaesthetized cats on blood glucose concentration of 25 μg adrenaline injected into different parts of the subarachnoid space. ●—● injection into the interpeduncular fossa; ○—○ injection, in another cat, into the cisterna terminalis. Injections at zero time.

between the optic foramina and the pituitary fossa. An injection of adrenaline into this space was followed by an immediate and sustained hyperglycaemia; subsequent injection of Evans blue produced intense staining of the inner surface of the dura in the anterior clinoid region. On the other hand, an injection of adrenaline into the pontine subdural space was ineffective, and the dye did not spread rostrally beyond the crest of the posterior clinoid process. The hyperglycaemic response to the injection of adrenaline into the subdural space rostral to the pituitary fossa is thus most

likely the result of absorption through the pars distalis of the pituitary. Although the pars distalis is not immediately accessible to adrenaline injected into the subarachnoid space, since this part of the pituitary lies outside the space, these experiments suggest the possibility of absorption of adrenaline from the subarachnoid space into the blood stream through the pars tuberalis of the hypophysis.

Injection of adrenaline into the cisterna magna after hypophysectomy

The results depended on whether or not the pars tuberalis was removed. When the hypophysectomy was complete, and the pituitary fossa was tightly packed with cotton wool, the hyperglycaemic response to intracisternally injected adrenaline was abolished; when only the gland but not the stalk was removed, it persisted. These results are shown in the first two lines of Table 3.

Table 3 includes, in line 3, a further series of five experiments in which in addition to complete hypophysectomy, a crater was made in the hypothalamus between the mammillary bodies and the chiasma, leaving a large area of injured tissue through which absorption could occur. In these experiments a hyperglycaemic response gradually developed.

The results of the six experiments summarized in line 2 of Table 3 show great variation between the extremes illustrated in Fig. 4. To explain this variation it is necessary to take into account that the hyperglycaemic response to intracisternal adrenaline consists of two components, absorption into the blood stream and a central action mediated by the splanchnic nerves (Sproull, 1963). The lower curve resembles the response previously obtained on intracisternal injection after bilateral splanchnicotomy, and may therefore be attributed mainly to absorption. Such a response was obtained in four of the experiments, and in each of them the cotton-wool used for packing the pituitary fossa pressed the torn edge of the arachnoid tightly on to the pia rostrally to the mammillary bodies, thus impeding access of the adrenaline to the caudal half of the tuber cinereum. It appears therefore that access of the adrenaline to the surface of the tuber cinereum beneath the pituitary stalk is necessary for the central component of the hyperglycaemic response to intracisternal adrenaline. The upper curve in Fig. 4 shows a hyperglycaemic response exceeding that usually seen after intracisternal injection of 50 μg adrenaline. Such a response was obtained in the other two experiments, and in both the pituitary fossa was only loosely packed with cotton-wool, so that the arachnoid was not pressed on to the pia over the tuber cinereum, and the adrenaline had free access to this region. The inadequacy of the packing during these two experiments was obvious, since the cerebrospinal fluid became blood-stained, which did not happen in the other four. Thus the

TABLE 3. Blood glucose concentrations of cats before and after the intracisternal injection of 50 μg adrenaline at zero time, showing the effects on the hyperglycaemic response of surgical interference with the hypophysial region

Preliminary operation	No. of cats	Time (min) −40	−20	0	+20	+40	+60	+80	+100
		Blood glucose concentration (mg/100 ml., mean ± S.D.)							
Complete hypophysectomy	3	83 ± 10	86 ± 12	94 ± 12	95 ± 11	97 ± 14	102 ± 13	107 ± 14	109 ± 14
Removal of the body of the pituitary gland	6	79 ± 7	83 ± 6	88 ± 9	142·5 ± 31	189 ± 35	208·5 ± 23	228 ± 39	235 ± 40
Complete hypophysectomy + excavation of hypothalamus	5	84 ± 7	85 ± 7	90 ± 10	103 ± 14	129 ± 14	167 ± 18	171 ± 24	181 ± 22

upper curve apparently represents a hyperglycaemia due to the central action as well as to the systemic absorption of adrenaline, and the enhancement of the response may be attributed to increased absorption of adrenaline through the wound made by cutting the pituitary stalk.

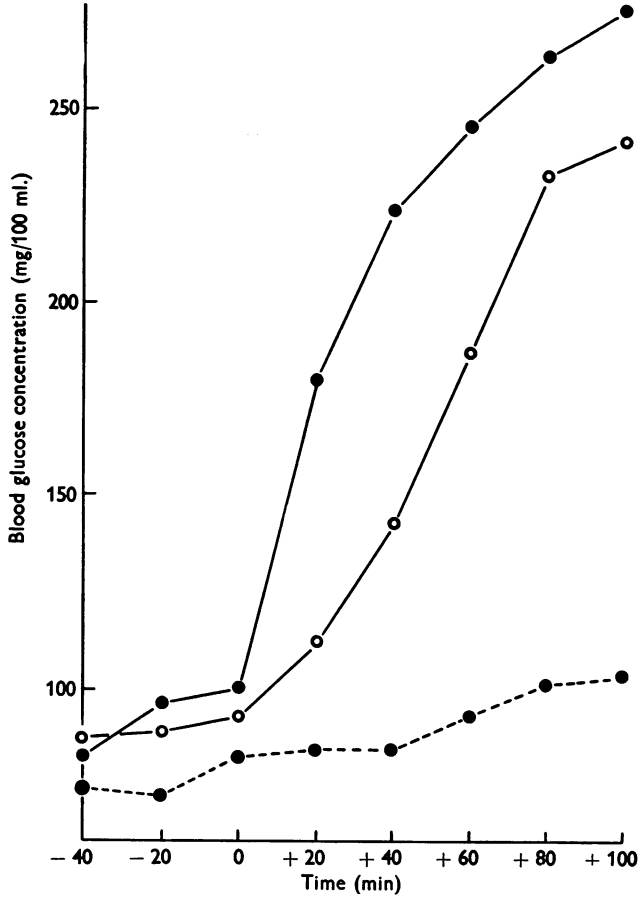

Fig. 4. Hyperglycaemic responses following the intracisternal injection of 50 μg adrenaline in three anaesthetized cats. Two show the greatest (●—●) and the least (○—○) responses after hypophysectomy below the stalk. The third curve (●----●) shows the abolition of the hyperglycaemic response after complete hypophysectomy. Adrenaline injections at zero time.

DISCUSSION

In previous experiments it was shown that the hyperglycaemic response to an intracisternal injection of adrenaline is accounted for partly by a central action mediated by the splanchnic nerves but mainly by absorption of adrenaline from the cerebrospinal fluid into the blood stream

(Sproull, 1963). The present experiments, carried out to locate the sites of the central action and of the absorption, show that the central action is on the caudal tuber cinereum, and the absorption is through the pars tuberalis of the hypophysis.

These sites are easily reached by the adrenaline, as demonstrated by the distribution of dye from the cisterna magna. Dye injected into the cisterna rapidly spreads along the ventral surface of the brain stem to the tuberal region. This spread is due to a rostral flow of the cerebrospinal fluid, from the foramina of Luschka ventrally into the cisterna pontis, through the interpeduncular fossa to the region around the circle of Willis, and then centrifugally along the main cerebral arteries. This rostral flow of cerebrospinal fluid, to and over the tuber cinereum, is also evident when dye is injected into the fourth ventricle or applied at different points in the subarachnoid space. The course of the flow is the same as that described in the intact system by Dott & Gillingham (1958). Under the present experimental conditions, after craniotomy and decompression of the cerebrospinal fluid, the flow is probably maintained by the pumping action in the sulci of the arterial pulse, which is increased after the subarachnoid space has been opened.

The rostral flow of cerebrospinal fluid, over the tuber cinereum and around the infundibulum, fully accounts for the fact that a given dose of adrenaline injected into the interpeduncular fossa produces a maximal hyperglycaemic response, yet injected into the cisterna terminalis produces no response. It is from these findings that the conclusion could be drawn that the sites both of the central hyperglycaemic action and of the absorption into the blood stream of intracisternal adrenaline lie on the ventral surface of the brain, between the interpeduncular fossa and the optic chiasma. These findings also, together with the hyperglycaemia seen after injection of adrenaline into the subdural space beneath the cisterna terminalis, led to the investigation of the effect of hypophysectomy on the hyperglycaemic response to intracisternal adrenaline.

Complete hypophysectomy abolished the hyperglycaemic response, but the results of partial hypophysectomy excluding the stalk varied, and the variation can be accounted for by anatomical features of the hypophysis in the cat. In this species the pituitary lies close to the mammillary bodies, from which it is separated by the subarachnoid space (Schwartz, 1936; Wislocki, 1937). The findings after partial hypophysectomy apparently depend on the tightness of the cotton-wool packing in the pituitary fossa after removal of the gland, which would affect the accessibility of the underlying surface of the caudal tuber cinereum to adrenaline in the subarachnoid space. When the pituitary fossa had been tightly packed, the splanchnic-mediated rapid onset of the central hyperglycaemia was

abolished. This did not happen when the packing was loose. The tight packing of the fossa had probably impeded the access of the adrenaline to the caudal tuber cinereum. If this interpretation is correct, the site of the central hyperglycaemic action of intracisternal adrenaline is on the tuber cinereum, between the mammillary bodies and the infundibulum.

The rostral and lateral surfaces of the pituitary stalk were not touched by the packing in the pituitary fossa after partial hypophysectomy, and the component of the hyperglycaemia attributable to systemic absorption was not affected by the extent and tightness of the packing. Since the systemic absorption of adrenaline persisted as long as the pituitary stalk remained, but was abolished after complete hypophysectomy, provided the underlying hypothalamus was not grossly injured, the absorption from the cerebral subarachnoid space must occur mainly through the pars tuberalis of the hypophysis. This would imply that absorption of adrenaline through the cerebral venous sinuses is not a factor in the hyperglycaemia seen after intracisternal injection of adrenaline. This is consistent with the finding that an injection into the cisterna terminalis of a dose of adrenaline, which is effective in the interpeduncular fossa, does not increase the blood glucose concentration. Adrenaline injected in this way reaches the venous sinuses of the cortex, as is shown by the distribution of the corresponding injection of dye. The failure of adrenaline to produce a hyperglycaemic response under this condition may be due to the constrictor effect of the amine on the cerebral veins, described by Forbes, Finley & Nason (1933).

The pars tuberalis of the hypophysis is a very vascular region in the subarachnoid space, outside the dense pia intima (Maximow & Bloom, 1957), and easily accessible through the cisterna magna. It is thus a likely site for the absorption of adrenaline from the cerebrospinal fluid. An intriguing implication of the present conclusion is that the blood vessels in this region must be relatively insensitive to the constrictor action of high concentration of adrenaline.

The present findings recall the suggestion of von Monakow (1921) that the cerebrospinal fluid may be a vehicle for local humoral agents, which implies the existence of absorptive regions. The pars tuberalis of the hypophysis might, on histological grounds, be such an absorptive region, and is strategically situated in the main stream of flow of the cerebrospinal fluid. The apparent capacity of the pars tuberalis to extract adrenaline from the cerebrospinal fluid therefore raises the question whether this structure may be concerned in the transport of other active substances from the cerebrospinal fluid to the hypophysis, hypothalamus and the blood stream.

SUMMARY

1. It has been shown previously that the hyperglycaemic response of the anaesthetized cat to intracisternal injection of adrenaline is due partly to a central action mediated by the splanchnic nerves but mainly to absorption of adrenaline into the blood stream.

2. It has now been shown, in experiments in which a given dose of adrenaline was injected into different regions of the subarachnoid space, that the site of the central hyperglycaemic action and that of the systemic absorption both lie on the ventral surface of the brain, between the interpeduncular fossa and the optic chiasma.

3. Experiments with intracisternal injection of adrenaline after complete and partial hypophysectomy suggest that the central action is on the tuber cinereum, between the mammillary bodies and the infundibulum, and point to the vascular pars tuberalis of the hypophysis as the site of the systemic absorption.

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