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CAROTID SINUS REFLEX AND CONTRACTION OF THE SPLEEN

BY

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A considerable number of studies (for references see Heymans, 1929a, b, and McDowell, 1938) have been made to determine the effect of stimulation of the carotid sinus by various means on different regions and organs of the body including the spleen, the organ with which the first part of this paper deals; the experiments we report were carried out in an effort to elucidate the mechanism mediating the contraction of the spleen caused by clamping the common carotid arteries.

Heymans (1929a), using dogs, found that clamping the carotids in one dog (A) brought about contraction of the spleen and a rise in blood pressure in a second dog (B, adrenalectomized) if there was an anastomosis between the adrenal vein of dog A and the jugular vein of dog B. The same result was obtained in dog B by inducing hypotension in the isolated and perfused carotid sinus of dog A (Heymans, 1929b). The conclusion was drawn that adrenaline secretion was reflexly stimulated by closing the common carotids and that this in turn brought about contraction of the spleen.

However, other authors were unable to reconcile the results of their experiments with this conclusion. Thelen (1933), Brauch (1934), and Euler and Liljestrand (1935) failed to demonstrate a rise in blood sugar level when the carotids were closed. The latter authors, however, believed that the adrenaline level in the peripheral blood was elevated during carotid occlusion. Holtz and Schümann (1949), employing dogs and cats, found that clamping the carotids caused a rise in blood pressure and contraction of the spleen but no rise in blood sugar level and no intestinal inhibition. Adrenaline used in doses just sufficient to produce the same splenic contraction as that caused by closing the carotids did, however, inhibit the intestine. Such was not the case with noradrenaline. Furthermore, ergotoxine or yohimbine abolished the rise in blood pressure caused by adrenaline but only slightly diminished the rise caused by noradrenaline or carotid closure. Clamping the carotids did not bring about splenic contraction in adrenalectomized animals, and these investigators were therefore led to the opinion that the contraction of the spleen, which they observed only before adrenalectomy, was the result of liberation of noradrenaline by the adrenal glands.

METHODS

Cats and dogs were anaesthetized with ether followed either by chloralose or pentobarbitone. The carotids were exposed in the neck, injections were made into the femoral vein, and the blood pressure was usually recorded from the femoral artery. The brachial artery was used instead when the abdominal aorta had been tied. The spleen volume

was recorded by connecting a plethysmograph to a piston recorder. In carrying out adrenalectomies, special care was taken not to damage the nerve supply to the spleen. Occasionally, the vagi were cut in the neck. This, however, did not greatly enhance the size of the blood pressure response to carotid occlusion.

The technique for collecting adrenal blood was usually that described by Feldberg and Minz (1934). In a few experiments, the animals were not eviscerated and the adrenal blood was obtained by inserting a piece of polythene tubing into the left lumbar vein. Care had to be taken to collect the adrenal blood without producing sensory stimuli which might lead to stimulation of the adrenal medulla. This was either achieved by continuous collection from the polythene tubing which was not moved during the whole procedure, or by using a by-pass of rubber tubing which returned the adrenal blood into a jugular or femoral vein when it was not required. The tubing could be opened and clamped at will without touching the animal. Heparin was used as anticoagulant; the blood was collected in ice, rapidly centrifuged, the plasma stored in the refrigerator and assayed as soon as possible on two or three different tissues. The samples were assayed against solutions of synthetic *l*-adrenaline and *l*-noradrenaline on the rat's uterus, the rat's colon (Gaddum, Peart, and Vogt, 1949), and the rat's blood pressure. Since the ratio of the sensitivity towards adrenaline and noradrenaline is about 150 for the rat's uterus and about 0.5 for the colon and the blood pressure, samples which cannot be distinguished on any of the three organs not only contain equiactive amounts of total base but must also contain the bases in equal proportions.

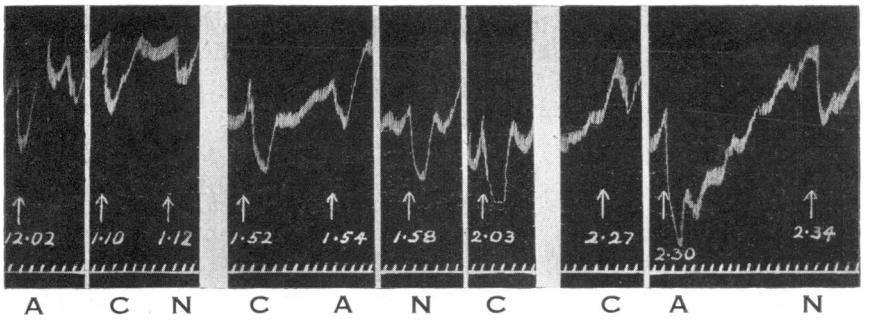
RESULTS

In a first set of experiments, the splenic contractions following carotid compression were compared before and after adrenalectomy and before and after section of the splenic nerves, most animals being subjected to both operations in succession. The effects were matched at the different stages of the experiment with the response to intravenous injections of adrenaline and noradrenaline. The results are recorded in Table I.

As might be expected, simultaneous extirpation of the adrenals and section of the splenic nerves abolished contraction (Cat 1). In two cats (2 and 9), mere cutting of the nerves had the same effect. In three cats (3, 4, and 5), adrenalectomy without section of the splenic nerves also abolished the contraction of the spleen. In these animals, however, the responses to adrenaline and noradrenaline were

TABLE I

Cat	Adrenalectomized	Splenic nerves cut	Splenic contraction on carotid closure
1	+	+	Abolished
2	0	+	Abolished
9	0	+	Abolished
3	+	0	Abolished
4	+	0	Abolished
5	+	0	Abolished
6	+	0	Diminished
	+	+	Abolished
7	+	0	Diminished
	+	+	Abolished
8	+	0	Unaffected
	+	+	Abolished



Cat No. 8, ♂, 2 kg. Ether, pentobarbitone. Record of spleen volume. Downward movement: contraction.

Time	Procedure	Rise in B.P. (mm. Hg)
12.02	3 μg. adrenaline i.v.	0
1.10	Carotids occluded for 30 sec.	18
1.12	3 μg. noradrenaline i.v.	17
1.30	*Adrenalectomy completed*	—
1.52	Carotids occluded for 30 sec.	27
1.54	3 μg. adrenaline i.v.	18
1.58	3 μg. noradrenaline i.v.	24
2.03	Carotids occluded for 30 sec.	22
2.15	*Splenic nerves cut*	—
2.27	Carotids occluded for 30 sec.	19
2.30	3 μg. adrenaline i.v.	16
2.34	3 μg. noradrenaline i.v.	19

A = 3 μg. adrenaline. C = Carotids occluded for 30 sec. N = 3 μg. noradrenaline.

It will be seen that the contraction of the spleen elicited by occlusion of the carotids is unaltered by adrenalectomy, but replaced by a passive dilatation after section of the splenic nerves.

FIG. 1

also abolished except to doses from 3 to 30 times those required to produce contraction before operation, an observation strongly suggestive of a change in the physiological state of the animals, most probably dehydration and hypothermia (rectal temperature 33°–34° C.). In operations on cats 6, 7, and 8, in which saline was infused and the rectal temperature was maintained at 35°–36.5°, the results were quite different. In these animals adrenalectomy did not prevent contraction, albeit in two (6 and 7) it diminished it, but the contraction was abolished by cutting the splenic nerves (Fig. 1). Hence, in order to get contraction of the spleen it is necessary that the nerves to the organ be intact, whereas the presence of the adrenals is not essential.

Stimulated by the observation of Meier and Bein (1948) that vasomotor responses to adrenaline injections in the hind limb of the adrenalectomized dog or cat were affected by infusion of noradrenaline, we instituted a second type of investigation. In 13 experiments on 5 adrenalectomized cats (1, 4, 5, 6, and 7) in which the spleen had ceased to respond to carotid occlusion, adrenaline alone, noradrenaline alone, and sometimes both together, were infused (at rates just insufficient to produce contraction), in order to see whether a high blood level of these compounds was

necessary for an otherwise unresponsive spleen to contract with closure of the carotids. In only one instance (cat 4) was there a restoration of activity. In this cat, noradrenaline in a concentration of 1 μg./c.c. of saline had been infused for 83 min. The fact that similar results were seen with saline alone, however, suggests that this result was due to the saline infusion *per se* rather than to the noradrenaline that was in the infusate.

In a third method of attack on this problem the quantity of adrenaline-like bases in blood collected from the adrenal veins of cats and dogs was estimated. The amounts found during a test period of intermittent carotid closure were compared with those secreted in control periods of steady blood pressure immediately before and after the test period. Since any fall in general blood pressure causes an acceleration of the release of " adrenaline," it was essential that the periods compared should have identical blood pressure baselines. In dogs, this was easily achieved because the blood volume was large compared with the amount of adrenal blood removed. In cats, infusion of dextran or of adrenaline-free blood from a splanchnotomized donor cat had often to be made in order to minimize the effect of collecting samples of adrenal blood. Comparisons of the " adrenaline " content of test and control samples of adrenal blood were made on 5 cats and 3 dogs. In none of the cats and in only one of the dogs did a detectable increase in the output of " adrenaline " result from clamping the carotids. The dog was in chloralose anaesthesia and had not been eviscerated. The " adrenaline " released during carotid occlusion was about 1.7 times that found in the plasma both before and after, and the increase was the same for the three tissues on which the samples were tested. Nevertheless, no such rise occurred in a second dog under apparently precisely the same experimental conditions.

Discussion

The foregoing experiments on cats show that the contraction of the spleen caused by occlusion of the carotid sinuses is abolished by section of the splenic nerves. It is not, however, abolished by adrenalectomy, provided the general condition of the animal, particularly with regard to blood pressure and blood volume, is satisfactory. It is possible that failure of other workers in this field to obtain a reaction of the spleen after adrenalectomy was due to a deterioration in the condition of the animal.

The fact that the contraction of the spleen will occur even if the adrenals have been removed does not exclude the possibility that release of adrenaline or noradrenaline takes part in the pressor effect due to hypotension in the carotid sinuses. In the present experiments, however, no proof of release of any such substance from the adrenal medulla of the cat could be obtained under a variety of conditions. The tests used for the assay of sympathomimetic amines would have shown an increase in total base as well as a shift in the percentage of methylation. Neither occurred in the cat, provided the precaution was taken to avoid a fall in blood pressure during the collection of samples.

In dogs, an increase in total sympathomimetic amines released during carotid occlusion was found in one experiment only, in spite of the fact that the rise in blood pressure obtained in this animal was by no means larger than in the other

two. Even in the dog, therefore, hypotension in the carotid sinuses may cause its effect on the blood pressure without a contribution by increased secretion from the adrenal medulla.

SUMMARY

In cats under sodium pentobarbital anaesthesia closure of the carotid arteries causes contraction of the spleen. This effect is reflexly mediated by the splenic nerves, and if these nerves are intact the contraction may occur whether or not the animal is adrenalectomized.

Occlusion of the carotids did not produce a shift in the ratio adrenaline/noradrenaline in adrenal plasma, and, except for one experiment on a dog, no evidence was obtained that it increased the output of adrenaline-like substances by the adrenal medulla.

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