HAS NORADRENALINE A DEPRESSOR ACTION IN THE NORMAL ANIMAL ?

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Received March 20, 1951

In their classical study of the relation between chemical structure of amines and their sympathomimetic action, Barger and Dale[1] noted that a dose of ergotoxine sufficient to reverse the pressor effect of *dl*-adrenaline in the spinal cat did not reverse that of *dl*-noradrenaline. Recent experiments in man (Goldenberg *et al.*[2], and Barcroft and Konzett[3]) show that, whereas noradrenaline causes a rise in systolic and diastolic pressure with a slowing of the heart rate, adrenaline causes a smaller rise in the systolic pressure and a fall in the diastolic pressure with the quickening of the heart rate. When infused intravenously, therefore, adrenaline causes a decrease of the general peripheral resistance, whereas noradrenaline causes an increase. In the cat under ether, with both vagi cut, Burn and Hutcheon[4] have shown that slow intravenous infusions of adrenaline produce a fall of blood pressure but those of noradrenaline produce a slight rise. When the volume of one hind leg (chronically denervated) is recorded, adrenaline produces dilatation whilst noradrenaline produces constriction. In the majority of cats, the depressor action of noradrenaline seen after giving ergotoxine or ergotamine is feeble or absent unless large doses are given (West[5]) but in occasional cats it is just as great as that of adrenaline (Burn and Hutcheon[4]). In addition, during perfusion of the rabbit ear with 2-benzylimidazoline, noradrenaline is dilator when adrenaline is dilator[4].

The present paper is concerned with the depressor action of noradrenaline noted in one spinal cat before the administration of an adrenaline antagonist. It has occurred in only one out of 98 preparations. Although the result is exceptional, it suggests that this action may be masked by a more powerful pressor component in the general preparation.

Results

The cat used in this study was a spinal preparation arranged as Burn, Hutcheon and Parker[6] suggest for the assay of noradrenaline and of adrenaline in mixtures of the two substances. In this technique, the two carotid arteries are not ligated before destruction of the brain, but one is cannulated afterwards for recording blood pressure. Doses of the amines are injected by the femoral vein. For this experiment, the blood pressure was set at a high level by using the animal immediately after destruction of the brain and cannulation. When adrenaline was given, the fall recorded in Fig. 1A was produced. This was the usual fall seen when the blood pressure is high and the dose of adrenaline is small (Moore and Purinton[7]). When 5 μg. of *l*-noradrenaline was injected, its vasodilator property was definite and well defined; increasing the dose

produced a larger well-sustained fall in blood pressure. This unexpected observation was further investigated.

After a rest of 20 minutes, the blood pressure fell from 120 mm. Hg. to about 80 mm. Hg. and the depressor actions of both adrenaline and noradrenaline were reduced (Fig. 1B). Several times later, successive doses of noradrenaline raised the pressure to about 106 mm. Hg., and

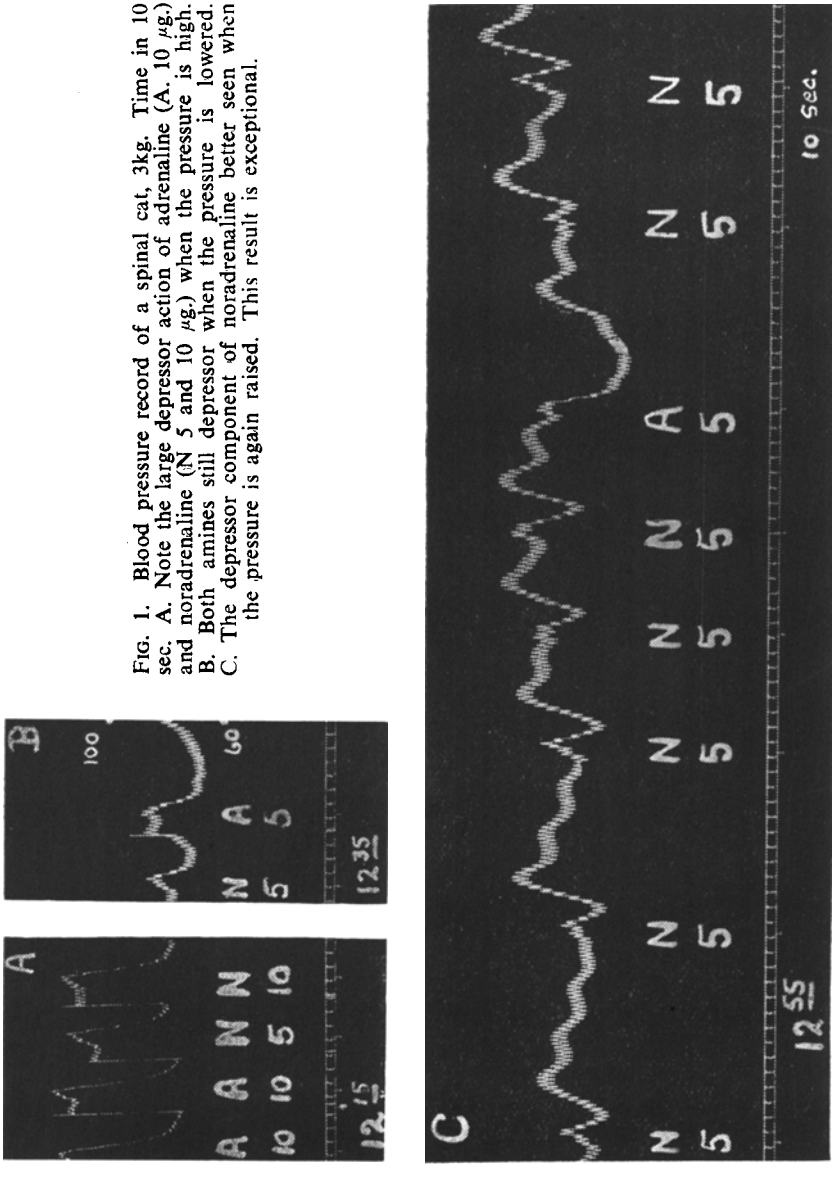
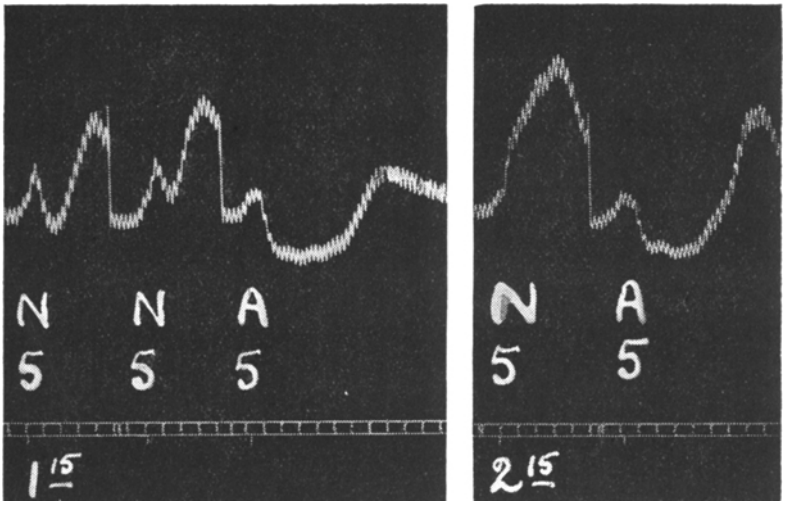


FIG. 1. Blood pressure record of a spinal cat, 3kg. Time in 10 sec. A. Note the large depressor action of adrenaline (A. 10 μg.) and noradrenaline (N 5 and 10 μg.) when the pressure is high. B. Both amines still depressor when the pressure is lowered. C. The depressor component of noradrenaline better seen when the pressure is again raised. This result is exceptional.

then the next noradrenaline dose produced a pure fall in pressure (Fig. 1C). Subsequent small doses of adrenaline (producing a biphasic response) and noradrenaline (pressor action only) followed the pattern of



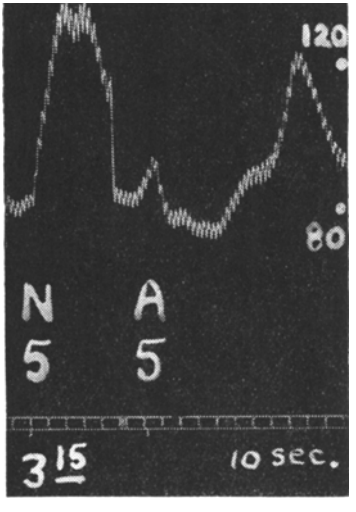


FIG. 2. Record as in Fig. 1. Later in the experiment, noradrenaline is purely pressor in action; adrenaline is biphasic.

effects mostly seen in spinal cat preparations (Fig. 2). Larger doses of the two amines were only pressor at a later stage.

DISCUSSION

It is generally accepted that adrenaline causes vasodilatation (a) in the cat under ether when the blood pressure is high because the vagi have been cut, and (b) in the cat to which ergotoxine or some other reversing

agent has been given. Burn and Hutcheon's observations appear to indicate that these two conditions are not the same, since noradrenaline does not cause vasodilatation in the cat under ether, whereas it causes dilatation in the rabbit ear vessels (and sometimes in the spinal cat) in the presence of a reversing agent exactly as does adrenaline. Noradrenaline does not dilate the vessels of the denervated hind leg of the cat; but rather it constricts them, the difference being probably confined to the muscle vessels. But, in direct contrast to this finding, McDowall[8] using skinned hind limbs in cats reported that both adrenaline and noradrenaline cause a dilatation of the vessels of the muscles.

Our result also casts doubt on Burn and Hutcheon's conclusion, in that both adrenaline and noradrenaline have been shown to possess depressor components in the normal animal. It may well be that the action of noradrenaline is similar to that of adrenaline (in similar doses) in dilating not only the coronary vessels of the cat and the dog, the intestinal vessels of the cat, and the vessels of the rabbit ear in the presence of a reversing agent (Burn and Hutcheon), but also in dilating the vessels of skeletal muscle or the intestinal vessels[9]. Usually this depressor action of noradrenaline is masked, and the blood pressure is raised.

Conclusion

In one spinal cat preparation, small doses of both adrenaline and noradrenaline possessed depressor components when the blood pressure was high. After a period of time, the pressor components of both amines predominated. The signficance of this finding is discussed.

References

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