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The action of desipramine on noradrenaline depletion by reserpine in the vas deferens of the rat *in vivo*

The interaction between reserpine and desipramine at the level of adrenergic neurons (both in the central and in the peripheral nervous system) has been investigated by many authors. Although desipramine does not block the reserpine-induced depletion of endogenous noradrenaline in brain or heart (Brodie, Bickel & Sulser, 1961; Garattini, Giachetti & others, 1962; Pletscher & Gay, 1962; Sulser, Watts & Brodie, 1962; Stone, Porter & others, 1964), it does significantly reduce the rate at which reserpine releases noradrenaline from these tissues (Manara, Sestini & others, 1966; Manara, Algeri & Sestini, 1967; Sulser, Owens & others, 1969). Desipramine was also shown to inhibit the release of tritiated noradrenaline by small doses of reserpine from prelabelled mice hearts (Titus, Matussek & others, 1966).

In the present study, another peripheral organ, the vas deferens, was used because of its rich adrenergic innervation and its high noradrenaline content (Sjöstrand, 1965). Sprague Dawley rats, 200 g, were given desipramine 15 mg/kg, i.p. 1 h before reserpine and the animals were killed at selected times after reserpine. Noradrenaline measurements were made in the heart and in the vas deferens (Shore & Olin, 1958).

Four vasa deferentia were pooled for each sample. The releasing action of reserpine is not very much affected by the pretreatment with desipramine (Table 1). However, at some times and doses, desipramine pretreated animals show a lower concentration of noradrenaline in the vas deferens compared with controls given only reserpine. Fig. 1 shows noradrenaline levels determined simultaneously in the heart and in the vas deferens of the same animals. It is evident that while in the heart, as previously reported (Manara & others, 1966), desipramine counteracts the noradrenaline releasing action of reserpine, in the vas deferens desipramine rather facilitates the depletion of noradrenaline.

The reason for the discrepancy observed in these two organs may lie in differences in their pattern of innervation, (Sjöstrand, 1965), blood flow (Kopin, Gordon & Horst, 1965), or enzymatic activity (Svihovec & Weiner, 1967). In fact, it has been shown that in organs which have short adrenergic neurons, such as the vas deferens, the rate of noradrenaline release induced by reserpine is different from that of organs innervated by long adrenergic neurons such as the heart (Owman & Sjöberg, 1967; Sjöstrand & Swedin, 1968).

Table 1. *Effect of desipramine* (DMI) *on the release of noradrenaline induced by reserpine in the rat vas deferens*

Treatment	Dose mg/kg i.v.	Vas deferens noradrenaline (μg/g) ± s.e. determined at various times after reserpine			
		30′	60′	120′	240′
Reserpine	1	7·6 ± 0·3	6·4 ± 0·1	4·5 ± 0·5	2·3 ± 0·3
§DMI + Reserpine	1	7·5 ± 0·3	6·3 ± 0·4	4·2 ± 0·4	1·5 ± 0·1
Reserpine	2·5	8·0 ± 0·4	5·3 ± 0·6	2·6 ± 0·1	1·3 ± 0·2
§DMI + Reserpine	2·5	6·6 ± 0·5*	5·5 ± 0·8	2·5 ± 0·6	1·0 ± 0·1
Reserpine	5	6·3 ± 0·2	4·2 ± 0·5	1·7 ± 0·3	0·9 ± 0·09
§DMI + Reserpine	5	5·2 ± 0·1†	4·2 ± 0·4	1·9 ± 0·3	0·6 ± 0·1
Reserpine	10	4·3 ± 0·3	3·2 ± 0·2	1·1 ± 0·07	
§DMI + Reserpine	10	4·5 ± 0·4	2·5 ± 0·1*	1·0 ± 0·02	
—		8·3 ± 0·2‡			
§DMI —			8·6 ± 0·3		

* $P < 0.05$.

† $P < 0.01$.

‡ Control values are the average of 29 experiments.

§ DMI (Desipramine) was injected i.p. 1 h before reserpine (Serpasil) at the dose of 15mg/kg. Numbers of experiments varied between 4 and 6 in each group.

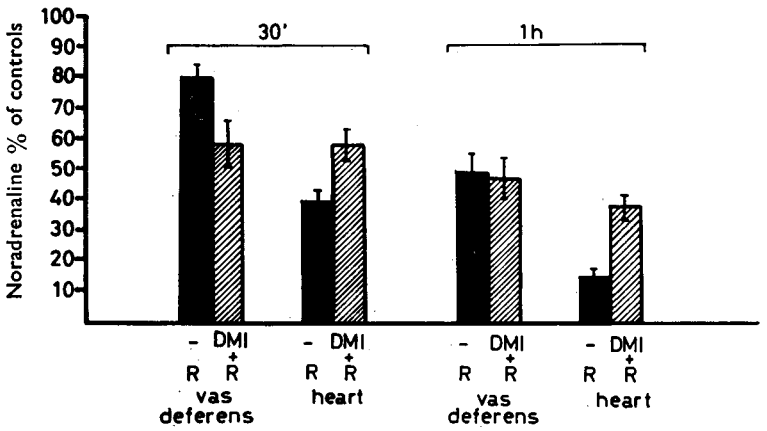

FIG. 1. Noradrenaline levels ± s.e. in heart and vas deferens after reserpine (R) and DMI + reserpine (DMI + R). Animals were killed 30 and 60 min after the i.v. injection of reserpine (2·5 mg/kg). Desipramine was given 60 min before reserpine at the dose of 15 mg/kg i.p. (Each column is the average of 4 determinations.)

Recently, Maître & Staehelin (1968), studying the effect of desipramine on the uptake of noradrenaline by various sympathetically innervated organs *in vivo*, showed that while the uptake of noradrenaline in the heart of the rat was inhibited by desipramine, it was "unexpectedly" enhanced in the vas deferens.

Taking into account these observations, it may be suggested that part of the noradrenaline released by reserpine from the vas deferens again enters into the nerve endings. Should the process of uptake be increased by desipramine, more noradrenaline would be available for MAO and therefore the concentration of noradrenaline would be reduced in animals given only reserpine.

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