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The effect of hemicholinium on the depletion of catecholamine induced by reserpine

SIR,—Reserpine-induced depletion of catecholamines from the adrenal medulla has been attributed both to a direct effect on the organ and to an effect secondary to stimulation of centres in the central nervous system (CNS). Callingham & Mann (1958) and Stjärne & Schapiro (1959) concluded that the depletion was due to a direct action on the organ, while Brodie, Olin, Kuntzman & Shore (1957), Holzbauer & Vogt (1956) and Mirkin (1961) showed that depletion occurred only indirectly. In the experiments demonstrating a direct effect, rats were used, whereas in those indicating the involvement of a neural component rabbits were most often used. It is possible that the differing results are explainable by a species difference.

Feldberg, Minz & Tsudzimura (1934) have shown that acetylcholine is the neurotransmitter liberated during splanchnic stimulation of the adrenal gland. Recent work in our laboratory (Stitzel, Campos & Shideman, 1965) has indicated that hemicholinium (HC-3), an inhibitor of acetylcholine synthesis, mimics the effect of splanchnic nerve section and impairs the depleting action of reserpine in rabbits. A similar experimental design is now used to examine the extent of CNS stimulation in the depletion caused by reserpine of catecholamines from rat adrenal medulla.

TABLE 1. EFFECT OF HEMICHOLINIUM (HC-3) ON RESERPINE-INDUCED CHANGES IN CATECHOLAMINE CONCENTRATIONS IN TISSUES OF THE RAT AND RABBIT. The results are based on 4–7 measurements and are expressed as means ± s.e.m. The heart and brain levels are expressed as μg/g of tissue, while those of the adrenal gland are expressed as μg/gland. For experimental details see text.

Treatment	Heart	Brain	Adrenal
Rats			
Control	0·99 ± 0·05	0·51 ± 0·07	22·3 ± 0·02
Reserpine	0·27 ± 0·04	0·33 ± 0·05	14·3 ± 0·03
HC-3 + Reserpine	0·20 ± 0·08	0·28 ± 0·07	12·0 ± 0·05
Rabbits*			
Control	2·13 ± 0·10	0·64 ± 0·10	83·8 ± 8·9
Reserpine	0·40 ± 0·05	0·20 ± 0·02	26·0 ± 7·0
HC-3 + Reserpine	0·41 ± 0·09	0·20 ± 0·03	67·1 ± 7·6

* Taken from the data of Stitzel & others (1965).

Male Sprague-Dawley rats weighing 200–300 g were given HC-3 (50 μg/kg) in three doses at intervals of 2 hr, beginning 1 hr before the injection of reserpine (5 mg/kg, i.p.). The first dose was given intraperitoneally and the second and third subcutaneously. Animals were killed by a blow on the head 2 hr after the last dose of HC-3 (i.e. 5 hr after reserpine). The adrenals, heart and brain stem were removed, weighed and homogenized in 0·01N hydrochloric acid. The catecholamine content in these tissues was measured spectrophotofluorometrically by the trihydroxyindole method of Shore & Olin (1958).

Reserpine greatly decreased the amine content of the heart and brain stem and pretreatment with HC-3 failed to affect this depletion (Table 1). These results are in complete agreement with our previous experiments with rabbits. Table 1 shows that reserpine also reduced the total amine content of the rat adrenal gland and that this effect could not be antagonized by HC-3. It is apparent, therefore, that not even this maximally tolerated dose of HC-3 could impair the amine-depleting action of reserpine in the rat, whereas in the rabbit, adrenal amine loss was almost completely prevented. HC-3 alone had no effect on amine levels in any of the tissues examined of either of the species.

It appears that the discrepancies noted in the literature can be accounted for by a species difference. Our experiments support the hypothesis (Kroneberg & Schümann, 1957) that reserpine-induced depletion in the adrenal gland of the rat is due to a direct action of the drug on the gland, while in the rabbit reserpine appears to cause amine depletion only indirectly.

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