Sympathin E and Nor-Adrenaline

The demonstration of a substance in extracts of 'adrenergic' nerves which conforms in biological and chemical respects with nor-adrenaline (U. S. v. Euler. *Acta physiol. Scand.*, 1946, **12**, 73; *J. Physiol.*, 1946, **105**, 38; 1948 data, to be published) has actualized the question as to the relations between this substance and the sympathin E of Cannon and Rosenblueth (*Autonomic neuro-effector systems.* New York: Macmillan, 1937). A contribution to this discussion was recently published in *Science* (November 28, 1947, p. 520) by Marrazzi and Marrazzi.

The conception of an excitatory sympathin E was primarily based on the fundamental discovery that only excitatory effects were obtained on stimulation of certain sympathetic nerves. Since nor-adrenaline is a substance possessing similar properties, being predominantly excitatory in its actions (G. Barger and H. H. Dale. *J. Physiol.*, 1910, **41**, 19), it has been repeatedly suggested that it might be identical with the postulated sympathin E (Z. M. Bacq. *Ann. Physiol. Physicochim. biol.*, 1934, **10**, 467; U. S. v. Euler. *J. Physiol.*, 1946, **105**, 38; C. M. Greer, *et al.* *J. Pharm. exp. Therap.*, 1937, **60**, 108; 1938, 62, 189; R. L. Stehle and H. C. Ellsworth. *J. Pharm. exp. Therap.*, 1937, **59**, 114).

The conclusion reached by the Marrazzis that nor-adrenaline cannot be identical with sympathin E opens some questions of principal interest which may invite some discussion.

Obviously, the nor-adrenaline shown to be present in the nerves themselves cannot be the sympathin E of Cannon and Rosenblueth, in the meaning of these authors, for the following two reasons:

(1) It is present in, and can be liberated from, the adrenergic nerves themselves (U. S. v. Euler. 1948 data, to be published) and need not be formed secondarily in the effectors, as is assumed for sympathin E.

(2) It is predominantly but not exclusively excitatory (G. Barger and H. H. Dale. *J. Physiol.*, 1910, **41**, 19; U. S. v. Euler. *Acta physiol. Scand.*, 1946, **12**, 73; G. B. West. *J. Physiol.*, 1947, **106**, 418).

It should be observed, however, that sympathin E in its original meaning has never been prepared nor have its assumed properties been controlled in detail. The possibility that the active substance responsible for the observed actions is liberated directly from the nerves is hard to exclude, and, with regard to its purely excitatory action, it is easy to imagine that a weak inhibitory action could have been overlooked. This is illustrated by Fig. 1, which shows the effects of an extract from splenic nerves of cattle on the blood pressure and the uterus *in vivo* of the cat. With a moderate dose, corresponding to 1 μg of 1-nor-adrenaline (kindly placed at my disposal by M. L. Tainter), no action could be detected on the uterus, whereas larger doses evoked a small but definite inhibitory action.

We believe, therefore, that the actions described by Cannon and Rosenblueth and attributed to sympathin E are due to the substance shown to be present in adrenergic nerves, having the properties of nor-adrenaline. On the other hand, since there is so far no convincing evidence for the presence of a sympathin E different from nor-adrenaline, this former term should preferably be dropped as inadequate in the strict sense.

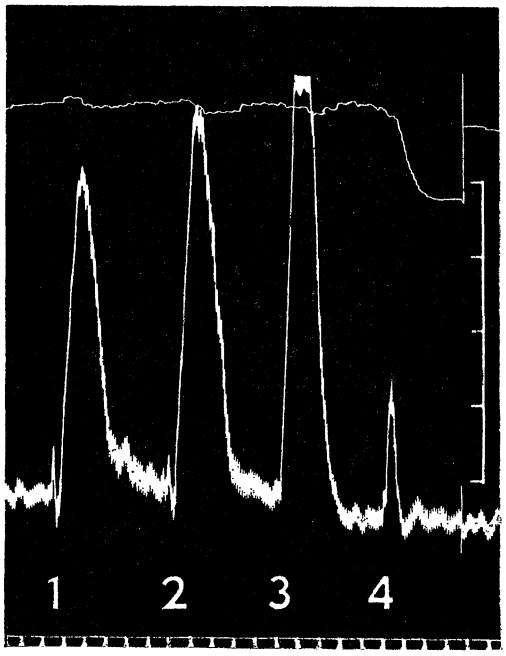

FIG. 1. Cat, chloralose. Gynergen, 0.1 mg/kg i.v.; atropine, 1 mg/kg s.c.; antergan, 5 mg/kg i.m. + 1 mg/kg i.v. Upper curve—movements of uterus; lower curve—blood pressure: (1) extract of 0.2 gm of splenic nerves, cattle; (2) extract of 0.3 gm of splenic nerves, cattle; (3) 3 μg of 1-nor-adrenaline hydrochloride; (4) 2 μg of 1-adrenaline hydrochloride. Time, 30 sec. Ordinate, B.P. 120–200 mm Hg.

The question whether adrenaline is liberated from certain kinds of adrenergic axones is not thoroughly clear, though the results of Gaddum and his co-workers (*J. Physiol.*, 1938, **94**, 87; 1939, **96**, 104, 385) strongly suggest such a possibility. If the term sympathin is taken to denominate any active sympathomimetic ergone liberated from 'adrenergic' axones, as recently proposed by Bacq and Fischer (*Arch. int. Physiol.*, 1947, 55, 73), it seems more satisfactory to use the distinctions sympathin N and sympathin A, which would then signify the transmitter having the properties of nor-adrenaline and adrenaline, respectively. This nomenclature would have the additional advantage of leaving place for any new kinds of similar transmitters.

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