THE ACTION OF *l*-NORADRENALINE AND ADRENOCHROME ON UNFATIGUED MAMMALIAN MUSCLE

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During the years 1947 to 1952 we have been interested in the ability of adrenaline to increase the maximal twitch tension of the unfatigued mammalian muscle. This effect is due to an action of adrenaline on the muscle fibre itself. We should like to give here a more precise report than has been published so far (9) on the following points: (1) the relative activity of *l*-adrenaline and *l*-noradrenaline; (2) the activity of adrenochrome on muscular contraction.

By close arterial injection to the tibialis anterior of the cat (3) we could confirm the finding of West and Zaimis (10) that noradrenaline is less efficient than adrenaline in producing a potentiation of the indirect maximal twitch. For instance, in one experiment 5 μg *dl*-noradrenaline induced potentiations of 3.2 and 1.6 per cent, whereas the corresponding values for 5 μg *l*-adrenaline were 5.0 and 6.1 per cent. A better estimation can be obtained from the isolated rat diaphragm preparation of Bülbring (4). In three different conditions (normal Tyrode, K-free Tyrode and K-free Tyrode with double Ca) the percentage increase in twitch tension produced by *l*-adrenaline 1×10^{-6} is greater than produced by *l*-noradrenaline 1×10^{-6}. If the activity of adrenaline is taken as 100 per cent, that of *l*-noradrenaline is 70.3 per cent. This conforms with the statement of Gaddum, Peart and Vogt (8) that "no tissue is known on which *l*-noradrenaline has much more effect than adrenaline, but various tissues are known on which it has much less action." For both sympathomimetic amines the activity is favoured by the lack of K^+ and an excess of Ca^{++} ions in the fluid surrounding the muscle. These results obtained from an isolated preparation offer no support for the hypothesis of West and Zaimis (10), namely that noradrenaline is less active than adrenaline on muscle in the whole cat, because it liberates less potassium from the liver.

The physiological properties of adrenochrome and its stable derivates have been reviewed in this journal, but reference to experiments on striated muscle were inadequate (1). It is beyond question that adrenochrome has a potentiating effect on the maximal twitch tension of the isolated rat diaphragm. The percentage increase in twitch tension produced by adrenochrome is about one-tenth of that of *l*-adrenaline. Similar experiments on the comparative activity of the semicarbazone of adrenochrome (adrenoxyl) and *l*-adrenaline show that the potentiating action of adrenoxyl 1×10^{-5} on the unfatigued muscle is inconstant, but that, when it is present it is of the same order as that of adrenochrome 1×10^{-5}. If the muscle is fatigued, by nerve stimulation at a frequency of 1 per sec., *l*-adrenaline, *l*-noradrenaline and adrenochrome, all of them at the concentration of 1×10^{-6}, exert a defatiguing action, which was never observed with adrenoxyl 1×10^{-5}. These experiments suggest that under certain circumstances the muscle is capable of hydrolyzing the adrenoxyl molecule and of setting free adreno-

chrome, which is active on muscle. The fact that on one or two occasions adrenoxyl increased markedly the maximal twitch tension should not be stressed, because it is an exceptional finding. The normal concentration of sympathomimetic substances in the blood (2, 7) is at or below threshold to exert an effect on muscular contraction (6). This action certainly comes into play when the suprarenals are vigorously stimulated in the conditions that W. B. Cannon called "emergency states." As the suprarenals liberate both *l*-noradrenaline and *l*-adrenaline (5), it was of interest to know the relative activity of these sympathomimetic amines on muscular contraction.

REFERENCES

1. Bacq, Z. M.: The metabolism of adrenaline. Pharmacol. Rev., 1: 1-26, 1949.
2. Blaschko, H.: Adrenaline and Sympathin. The Hormones, edited by Pinkus, G. and Thimann, K. V. Academic Press, New York, 2: 601-631, 1950.
3. Brown, G. L.: The preparation of the tibialis anterior (cat) for close arterial injections. J. Physiol., 92: 22P, 1938.
4. Bülbring, E.: Observations on the isolated phrenic nerve diaphragm preparation of the rat. Brit. J. Pharmacol., 1: 31-61, 1946.
5. Bülbring, E. and Burn, J. H.: Liberation of noradrenaline from the suprarenal gland. Brit. J. Pharmacol., 4: 202-247, 1949.
6. DeVisscher, M., Gerbault, J. and Fontenelle, E.: Thyroxine et réactions du muscle strié à l'adrénaline. Ann. endocrinol., 12: 1119-1121, 1951.
7. Euler, U. S. v.: Noradrenaline. Proceedings of the Second Biochemical Congress, Paris, 1952. Symposium sur les hormones protéiques et dérivées des protéines, pp. 39-55.
8. Gaddum, J. H., Peart, W. S. and Vogt, M.: The estimation of adrenaline and allied substances in blood. J. Physiol., 105: 467-481, 1949.
9. Goffart, M.: Recherches relatives à l'action de l'adrénaline sur le muscle strié de mammifère. Arch. internat. physiol., 60: 318-418, 1952.
10. West, G. B. and Zaimis, E. J.: A comparison of adrenaline and noradrenaline on mammalian muscle. J. Physiol., 110: 18P-19P, 1949.