In the guinea-pig myenteric plexus, morphine (1·33 μM) did not depress evoked NA output although the release of acetylcholine is depressed by this drug (Paton, 1957). In this tissue, the output of NA per pulse at 16 Hz was twice that at 2 Hz. Phenoxybenzamine (29·3 μM) increased the output 7-fold at both frequencies.

The different types of frequency-output relationships found in the various tissues may represent multiple mechanisms for the control of NA release. It may be significant that sensitivity to morphine appears to be linked with only certain types of frequency-output relationships both in the cholinergic (Greenberg, Kosterlitz & Waterfield, 1970) and adrenergic systems.

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REFERENCES

CAIRNIE, A. B., KOSTERLITZ, H. W. & TAYLOR, D. W. (1961). Effect of morphine on some sympathetically innervated effectors. *Br. J. Pharmac. Chemother.*, **17**, 539–551.

GREENBERG, R., KOSTERLITZ, H. W. & WATERFIELD, A. (1970). The effects of hexamethonium, morphine and adrenaline on the output of acetylcholine from the myenteric plexus-longitudinal muscle preparation of the ileum. *Br. J. Pharmac.*, **40**, 553–554*P*.

HUGHES, J. (1972). Evaluation of mechanisms controlling the release and inactivation of the adrenergic transmitter in the rabbit portal vein and vas deferens. *Br. J. Pharmac.*, **44**, 472–491.

KOSTERLITZ, H. W. & TAYLOR, D. W. (1959). The effect of morphine on stimulation of postganglionic sympathetic fibres. *J. Physiol., Lond.*, **149**, 59–60*P*.

PATON, W. D. M. (1957). The action of morphine and related substances on contraction and on acetylcholine output of coaxially stimulated guinea-pig ileum. *Br. J. Pharmac.*, **12**, 119–127.

THOMPSON, J. W. (1960). The cat's nictitating membrane as an isolated preparation. Ph.D. thesis, University of London.

TRENDELENBURG, U. (1957). The action of morphine on the superior cervical ganglion and on the nictitating membrane. *Br. J. Pharmac. Chemother.*, **12**, 79–85.

The effect of nerve stimulation on the depletion of noradrenaline by reserpine in the heart, vas deferens and anococcygeus muscle of the rat

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Most adrenergically innervated peripheral organs are depleted of their noradrenaline (NA) content by reserpine to a roughly similar degree. An exception is the vas deferens which is relatively resistant (Sjöstrand & Swedin, 1968). Two possible explanations are either that the rate of depletion is dependent on the firing frequency in the nerves and this is low in the vas deferens, or that 'short' adrenergic neurones in the vas deferens are less easily depleted than the long adrenergic neurones elsewhere. We have investigated these by studying the effect of artificial stimulation on the rate of depletion of the nerves to the heart, vas deferens and anococcygeus. The latter has a dense adrenergic innervation uniformly distributed throughout the muscle like the vas deferens, but unlike the vas deferens, the neurones are conventional 'long' ones (Gillespie & McGrath, 1972).

Rats were given various doses of reserpine intraperitoneally, the vas deferens and anococcygeus muscles removed 24 h later, and the NA content measured. A dose of 200 μg/kg caused 80–90% depletion of NA in both muscles. The time course of depletion with such a dose was then examined in all three organs. After 6 h

the heart was 90% depleted whereas the vas deferens and anococcygeus were only 50% depleted. This dose (200 μg/kg) and time (6 h) were selected to study the effects of nerve stimulation. Six groups of rats were used, control animals ; animals pithed but unstimulated ; animals pithed and the sympathetic nerves stimulated ; animals given reserpine but neither pithed nor stimulated ; animals given reserpine, pithed but not stimulated ; and animals given reserpine, pithed and stimulated. The appropriate spinal outflows were stimulated by a movable electrode in the spinal canal (Gillespie, MacLaren & Pollock, 1971).

The level of NA at 6 h in animals pithed but unstimulated rose in the anococcygeus muscle in comparison with the controls ; stimulation of the nerves at 30 Hz for 10 s periods at 90 s intervals for 2 h lowered NA levels in all organs. Reserpine alone caused a 50% reduction in the vas deferens and anococcygeus and a 90% reduction in the heart.

Pithing the animal after giving reserpine reduced the depletion in the vas deferens and anococcygeus to 36% and 42% respectively and in the heart to 66%. Stimulation of the nerves for 2 h in the reserpinized rat increased the depletion in the vas deferens and anococcygeus to 68% and 82% respectively, but in the heart simply restored the depletion to 90%. The increased depletion with nerve stimulation in the vas deferens and anococcygeus was statistically significant. Since the anococcygeus and vas deferens are equally resistant to reserpine depletion, the length of the adrenergic neurone seems to be unimportant. The reduced depletion, following pithing in all three tissues and the increased depletion by nerve stimulation in the vas deferens and anococcygeus suggest that impulse traffic is an important factor.

REFERENCES

GILLESPIE, J. S., MACLAREN, A. & POLLOCK, D. (1970). A method of stimulating different segments of the autonomic outflow from the spinal column to various organs in the pithed cat and rat. *Br. J. Pharmac.*, **40**, 257–267.

GILLESPIE, J. S. & MCGRATH, J. C. (1972). The origin of the inhibitory nerve pathway to the rat anococcygeus muscle. *J. Physiol., Proc. Phys. Soc. March.*

SJÖSTRAND, N. O. & SWEDIN, G., (1968). Effect of reserpine on the noradrenaline content of the vas deferens and the seminal vesicle compared with the submaxillary gland and the heart of the rat. *Acta Physiol. Scand.*, **72**, 370–377.

The effect of cations on the spontaneous and drug induced efflux of ^{3}H-L-noradrenaline from the mesenteric arteries

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Perfusion of the rat mesenteric artery preparation with Ca^{2+} and Mg^{2+} free Krebs solution potentiates the pressor responses to tyramine, octopamine, metaraminol and noradrenaline (George & Leach, 1971).

To investigate the mechanism of this potentiation, the rat mesenteric artery preparation was perfused with (−)-noradrenaline-7-^{3}H and carrier (−)-noradrenaline diluted with normal Krebs solution to give a final concentration of 0·42 μCi/ml ^{3}H-(−)-noradrenaline and 200 ng/ml noradrenaline respectively, using the precautions described by Iversen (1963). The mesentery was perfused with this solution