Secretion of adrenaline and noradrenaline from the perfused cat adrenal gland

E. MIELE and R. P. RUBIN*, *II Department of Pharmacology, Naples University, Italy, and Department of Pharmacology, State University of New York, Downstate Medical Center, Brooklyn, New York, U.S.A.*

Cat adrenal glands were perfused with Locke solution and the release of adrenaline (A) and noradrenaline (NA) was measured under different conditions of stimulation and inhibition. The addition of nicotine (10^{-6}M) to the perfusion medium for 2 min periods elicited a mean catecholamine output of 5.57 ± 0.64 μg/min and $69.3 \pm 3.3\%$ was NA. Equipotent concentrations of pilocarpine (10^{-3}M), histamine (10^{-3}M) and potassium (17 mM) released a predominance of A (70–80%). Acetylcholine released approximately equal quantities of A and NA. Tetracaine inhibited preferentially the NA-dominant secretion induced by nicotine (Table 1). Only in high concentrations which block calcium flux (Rubin, Feinstein, Jaanus & Paimre, 1967) did tetracaine depress the catecholamine secretion elicited by pilocarpine (Table 1) and other agents which released a predominance of A. Tetracaine was not as effective against acetylcholine as it was against nicotine (Table 1). These results and those obtained from previous studies (Jaanus, Miele & Rubin, 1967; Rubin, Cohen, Harman & Roer, 1968) provide further evidence for the existence in the cat of two types of medullary chromaffin cells, which contain either A or NA and possess pharmacologically distinguishable characteristics.

TABLE 1

	Catecholamine output μg/min$\pm$S.E. (no. of expts)	NA (%)	ED 50 tetracaine
Nicotine ($1{\cdot}2\times10^{-6}$M)	$5{\cdot}57\pm0{\cdot}64$ (17)	$69{\cdot}3\pm3{\cdot}3$	$2{\cdot}9\times10^{-6}$M (4)
Pilocarpine (10^{-3}M)	$2{\cdot}05\pm0{\cdot}14$ (13)	$25{\cdot}8\pm2{\cdot}9$	$3{\cdot}4\times10^{-4}$M (3)
Acetylcholine (6×10^{-6}M)	$4{\cdot}86\pm0{\cdot}44$ (20)	$54{\cdot}4\pm0{\cdot}53$	$4{\cdot}6\times10^{-5}$M (5)

REFERENCES

JAANUS, S. D., MIELE, E. & RUBIN, R. P. (1967). The analysis of the inhibitory effect of local anaesthetics and propranolol on adrenomedullary secretion evoked by calcium or acetylcholine. *Br. J. Pharmac. Chemother.*, **31**, 319–330.

RUBIN, R. P., FEINSTEIN, M. B., JAANUS, S. D. & PAIMRE, M. (1967). Inhibition of catecholamine secretion and calcium exchange in perfused cat adrenal glands by tetracaine and magnesium. *J. Pharmac. exp. Ther.*, **155**, 463–471.

RUBIN, R. P., COHEN, M. S., HARMAN, S. M. & ROER, E. (1968). The localization of adrenaline-rich medullary chromaffin cells adjacent to the adrenal cortex. *J. Endocr.*, in the Press.

Non-specific inhibitory effects of morphine-like drugs on transmission in the superior cervical ganglion and guinea-pig isolated ileum

H. W. KOSTERLITZ, G. M. LEES*, D. I. WALLIS and A. J. WATT, *Department of Physiology, University of Aberdeen, Scotland*

It has been shown on many occasions that morphine-like compounds inhibit the responses of certain autonomic effectors to stimulation of their nerves at low frequencies. The inhibitory effect of morphine (ID50 = 0.07 μM) on the responses of the longitudinal muscle of the guinea-pig isolated ileum to coaxial electrical stimulation is antagonized by naloxone (N-allylnoroxymorphone); a dose ratio of 2 is

obtained with a concentration of 0.0012 μM, at which concentration naloxone has no agonist activity (Kosterlitz & Watt, 1968).

Recently, however, we have found that in very high concentrations (50–100 μM), naloxone causes a depression of the twitch induced by coaxial stimulation. These high concentrations reduce the responses of the longitudinal muscle also to agents which act directly on the smooth muscle cells—for example, acetylcholine, histamine and bradykinin; thus the depressant action of naloxone, unlike that of low concentrations of morphine (Paton, 1957), cannot be attributed to a reduction of acetylcholine release. Furthermore, the recovery from the antagonist action of a low concentration of naloxone has a half-time of 19 min, whereas the depressant effect of a high concentration of naloxone is fully reversed 6 min after washing out the drug.

In rabbit isolated superior cervical ganglia, in which transmission was just blocked by hexamethonium (275–550 μM), relatively high concentrations of morphine (27–130 μM) are required to depress the synaptic potential; this depression is reversed by naloxone (3–7 μM). In high concentrations (100–300 μM) naloxone itself had a depressant effect which was partly reversed by washing out the drug.

In the perfused superior cervical ganglion of the cat, morphine (130–2,700 μM) causes a decrease in the contraction of the nictitating membrane in response to stimulation of the preganglionic nerve; this effect is only partly due to a reduction in acetylcholine output. The depressant effects of morphine on acetylcholine release and on transmission are reversed 2–5 min after changing to a morphine-free Krebs solution. The block of transmission is not antagonized by naloxone which, in concentrations of 400–700 μM, blocks transmission as effectively as morphine.

On the basis of these results, it is suggested that care must be taken to differentiate specific from non-specific inhibitory actions of morphine-like compounds when these are used in high concentrations.

This investigation was supported in part by U.S. Public Health Service Grant NB 03026.

REFERENCES

KOSTERLITZ, H. W. & WATT, A. J. (1968). Kinetic parameters of narcotic agonists and antagonists, with particular reference to N-allylnoroxymorphone (naloxone). *Br. J. Pharmac. Chemother.*, **33**, 266–276.

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

The human isolated vas deferens: its response to electrical stimulation and to drugs

A. T. BIRMINGHAM, *Department of Pharmacology, King's College, Strand, London, W.C.2, England*

Both vasa deferentia were removed by vasectomy under general anaesthesia from healthy young men (aged between 33 and 41 years) and transported in cold Krebs solution to the laboratory. When suspended between parallel platinum wires (Birmingham & Wilson, 1963) in Krebs solution at 32° C bubbled with 95% oxygen and 5% carbon dioxide, electrical stimulation (0.1 msec pulse duration; maximal voltage) induced a threshold contraction at 2 shocks/sec and an increased height