Desensitization of the rat aortic strip to vasopressin by infusions of noradrenaline

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Eden & Nasmyth (1974) showed that when noradrenaline (400 ng kg^{-1} min^{-1}) was perfused for 30 min through an organ bath containing a rat aortic strip bathed in Krebs solution, it desensitized the tissue to noradrenaline. In order to determine whether or not the desensitization was specific for noradrenaline, the experiment was repeated using vasopressin as the agonist.

Responses of the rat aortic strip to vasopressin (1.5–2.5 mU ml^{-1}) were established before and after perfusing the organ bath with noradrenaline (400 ng kg^{-1} min^{-1}) for 30 min, the rate of infusion being based upon the weight of the animal from which the aorta had been removed. In four experiments the responses to vasopressin were reduced by 65–80% with a mean of 74%.

To determine if the β-adrenoceptors were involved in the phenomenon, the experiment was repeated with propranolol (3.3 μM) in the Krebs solution bathing the tissue. It was without effect on the responses to vasopressin and it did not prevent the desensitization produced by the infusion of noradrenaline. When phentolamine (5–7 μg kg^{-1} min^{-1}) was infused together with the noradrenaline, the response to the latter was blocked. Thirty minutes after stopping the infusion of both drugs, but continuing to perfuse Krebs solution through the organ bath at the rate of 10 ml min^{-1}, the responses to noradrenaline were fully restored and those to vasopressin were unaffected. Thus blockade of the α-adrenoceptors prevented the desensitization.

It was established that clonidine, which stimulates presynaptic α-adrenoceptors preferentially (Starke, Montel, Gayk & Merker, 1974), was 100 times less effective than noradrenaline on post-synaptic α-adrenoceptors in this tissue. Phenylephrine, which stimulates post-synaptic α-adrenoceptors preferentially (Starke, Endo & Taube, 1975) was equipotent with noradrenaline on these receptors.

When infusions of clonidine varying from 450 ng to 2.5 μg kg^{-1} min^{-1} were employed the responses to vasopressin in 5 experiments were reduced by 43–77% with a mean of 56%. Infusions of phenylephrine (52 μg kg^{-1} min^{-1}) reduced the responses to vasopressin by 24–40% with a mean of 32% in 4 experiments.

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Effects of catecholamine antagonists on the milk-ejection reflex of the anaesthetized rat

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The 'oxytocinergic' neurones of the supraoptic and paraventricular nuclei of the lactating rat display a rapid burst of action potentials (> 40 Hz, 2–4 s) every 5–15 min during suckling (Lincoln & Wakerley, 1975). This burst of neuronal activity releases a pulse of oxytocin (~ 1 mU) from the neurohypophysis; this circulates to the mammary glands, contracts the myoepithelial cells and ejects the milk. Catecholamines may be involved in the central control of this neuroendocrine reflex for both noradrenaline and dopamine release oxytocin and vasopressin when placed in the lateral ventricles of the brain (Kuhn, 1974; Bridges, Hillhouse & Jones, 1975). This study examines the effects of antagonists of noradrenaline and dopamine upon the milk-ejection reflex of the rat, for with the exception of the ergot alkaloids which prevent milk ejection in the conscious rat (Grosvenor & Turner, 1957) no such study has been reported.

Rats, from day 7–10 of lactation and separated from their young for 16 h, were anaesthetized with urethane (1.1 g/kg, i.p.) and the teat ducts of two mammary glands were cannulated to record intramammary pressure. Three hours later, and whilst the animals were still deeply anaesthetized, 10 pups were applied to the uncannulated nipples. Each milk ejection in the subsequent 3 h period of suckling was recorded; each ejection was associated with an abrupt rise in intramammary pressure and a concomitant