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RESPONSE OF THE CAT'S PAD ECCRINE SWEAT GLANDS TO INTRAVASCULAR INJECTIONS OF CATECHOLAMINES

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SUMMARY

1. Using a sensitive method for detecting and monitoring sweat secretion, a study has been made of the effects of adrenaline and noradrenaline on the cat's pad sweat gland activity in the anaesthetized cat.

2. Intravenous or intra-arterial injections of adrenaline or noradrenaline only very occasionally caused these glands to secrete.

3. The predominant effect of these drugs on glands which are already secreting in response to plantar nerve stimulation is inhibitory.

4. The catecholamine inhibition could be reduced or blocked by phentolamine, but not by propranolol, dibenamine or phenoxybenzamine.

5. It is concluded that these glands can be directly activated by intravascular injections of adrenaline or noradrenaline, but that the inhibitory effect of concomitant vasoconstriction usually prevents a response being detected at the skin surface.

INTRODUCTION

Human eccrine sweat glands will secrete in response to intradermal injections of noradrenaline or adrenaline. The responsiveness of cat's pad sweat glands to intradermal injections, on the other hand, is not so clearly demonstrable (Langley, 1922; Rothman, 1954). Further, Burn (1925) only obtained a response from the intravenous administration of adrenaline in the conscious cat if the innervation to the paw was intact. More recently, however, Lloyd (1959) has claimed that noradrenaline will activate the cat's pad sweat glands. Lloyd followed the activity of the glands by measuring impedance changes across the skin and did not measure the actual sweat output. Using a recently developed sensitive method (Foster, 1966) for monitoring sweat secretion, the response of the cat's pad sweat glands to the intravascular administration of noradrenaline and adrenaline has been studied.

METHODS

The sweat response was monitored by sticking a capsule, with inlet and outlet tubes situated at its base, on to the central portion of the central pad of the hind foot. (Capsules of similar design, but of different areas, were constructed, the area of the capsule used depending on the size of the pad. The areas of the capsules varied from approximately 0·2 cm^2 to approximately 0·5 cm^2.) To make the capsule secure a metal ring was fixed around the whole pad, and the small capsule was then clamped into position by means of four screws in the metal ring (fig. 1 in Foster, 1966).

The capsule was ventilated with dry nitrogen, and the nitrogen together with any evaporated sweat was then passed through an infra-red analyser and flowmeter (Fig. 1). The gas flow was varied from 0·1 to 1 l./min according to the secretion rate expected. The infra-red analyser has two ranges, the ratio of the sensitivities being 1 : 10. Calibration was carried out by introducing a known volume of water (usually 100 μl.) into a bypass circuit and using the least sensitive range of the analyser. For the measurement of sweat secretion the most sensitive range was used (full-scale deflexion being approximately 1·3 μl./min at 1 l./min gas flow), the volume or rate being determined by reference to the calibration curve after correcting for the sensitivity change and any change in gas flow.

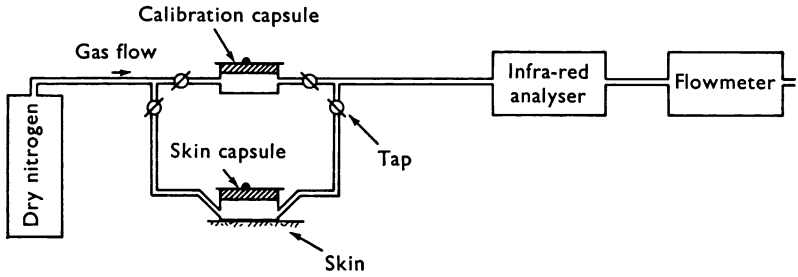

Fig. 1. Diagram of system used to monitor sweat response.

Cats were anaesthetized with intraperitoneally administered sodium pentobarbitone and drugs were administered either intravenously via the femoral vein of the opposite leg or into the anterior tibial artery leading directly to the glands.

When adrenaline or noradrenaline was administered to the resting glands the responsiveness of the glands was always previously tested either by nerve stimulation or the administration of mecholyl.

Nervous stimulation of the glands was carried out by means of 10 V stimuli of 1 msec duration applied to the lateral branch of the internal plantar nerve. This produces a constant response to stimuli at a constant frequency (Fig. 2).

RESULTS

Administration of catecholamines to resting glands

Noradrenaline or adrenaline (1 to 200 μg) given intravenously failed to produce a response in three cats.

A secretion occurred in only one cat out of five as a result of the arterial administration of noradrenaline or adrenaline (0·1–5 μg doses). This secretion decreased markedly with successive doses until no response was obtained at all (Fig. 3).

Catecholamine administration also tended to reduce the response to arterially administered mecholyl (Fig. 4).

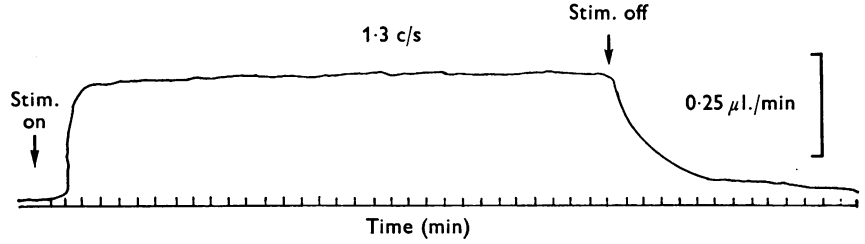

Fig. 2. Response of cat's foot pad sweat glands to a constant frequency of plantar nerve stimulation. Response measured by passing evaporated sweat from the central pad of the hind foot through an infra-red analyser.

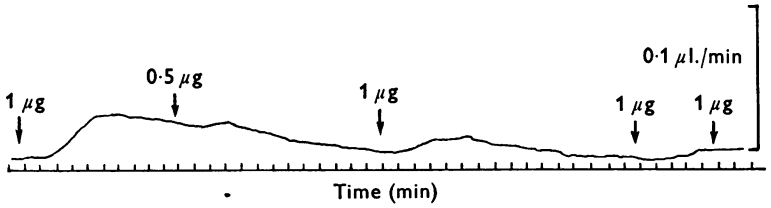

Fig. 3. Response of cat's pad sweat glands to repeated doses of arterially administered noradrenaline.

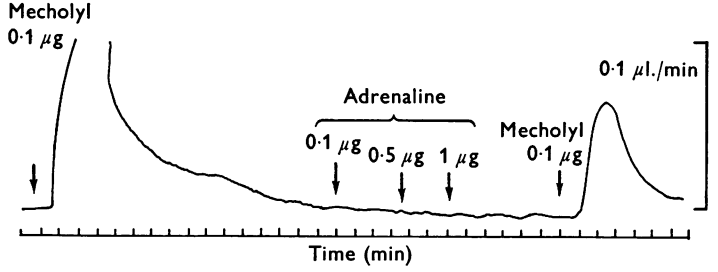

Fig. 4. Effect of adrenaline on response of cat's pad sweat glands to arterially administered mecholyl. Adrenaline also administered arterially.

Administration of catecholamines to activity secreting glands

(*a*) *During high frequencies of stimulation* (1–6/*sec*). Adrenaline or noradrenaline (25–50 µg intravenously or 0·5–5 µg arterially) given to ten cats always produced a marked inhibition which was usually followed by complete recovery of sweat rate (Fig. 5*a*). The inhibition was often preceded by a transient increase in the sweat rate (Fig. 5*b*).

(*b*) *During low frequencies of stimulation* (6–48/min). Adrenaline or noradrenaline (4–40 µg intravenously or 0·5–5 µg arterially) was given to six cats whilst stimulating at these frequencies. In two of these cats there

was either no response or a transient increase in rate. In the other four cats there was either no response or a transient decrease in rate.

There was no obvious difference between the effects of adrenaline and noradrenaline on the response of the glands and central ligation of the plantar nerve did not affect the response.

Effect of α- and β-adrenergic blockers on the catecholamine inhibition

(*a*) *Dibenamine and phenoxybenzamine.* Although dibenamine (20 mg/kg) and phenoxybenzamine (12–22 mg/kg) may have had some effect in reducing the catecholamine inhibition, this inhibition was still very marked after giving these drugs (Figs. 6, 7*b*). These substances were infused very slowly intravenously.

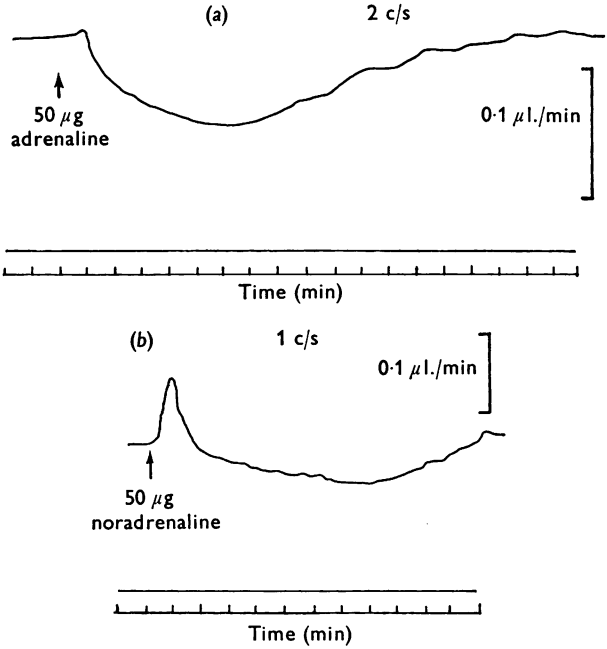

Fig. 5. Effect of catecholamines on the actively secreting cat's pad sweat glands. (*a*) 50 μg adrenaline intravenously whilst stimulating at 2 c/s. (*b*) 50 μg noradrenaline intravenously whilst stimulating at 1 c/s.

(*b*) *Propranolol.* There was no reduction of the catecholamine inhibition after giving 0·5–1·1 mg/kg doses of propranolol intravenously.

(*c*) *Phentolamine.* Phentolamine (1–3 mg/kg intravenously or 25–500 μg arterially) always significantly reduced and sometimes prevented the catecholamine inhibition (Fig. 7).

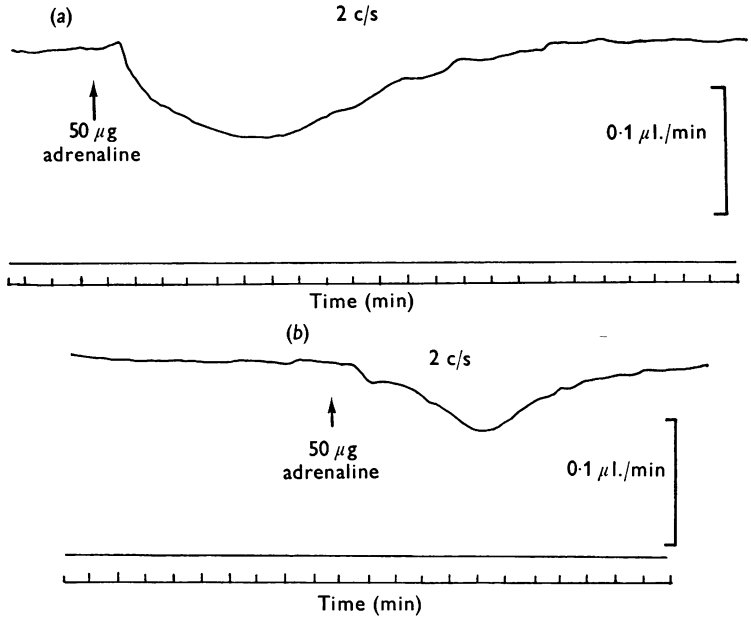

Fig. 6. Effect of 20 mg/kg dibenamine (intravenously infused over 16 min) on the adrenaline inhibition. (*a*) 50 μg adrenaline intravenously before dibenamine. (*b*) 50 μg adrenaline intravenously 1 hr after dibenamine administration.

DISCUSSION

The method used in these studies enables the detection of very small responses or changes in responses to be made, particularly at the lower gas flows used. A very wide range of doses of adrenaline or noradrenaline were given and frequently very young kittens (which had been observed to secrete in response to emotional stimuli whilst conscious) were used. In contrast to the human glands, therefore, only in a small minority of cases will the cat's pad glands secrete in response to these substances.

The predominant response of actively secreting glands whether the noradrenaline or adrenaline was administered intravenously or arterially was inhibitory. As transmission to these glands is completely blocked by small doses of atropine, it is unlikely that there is an activating adrenergic component in their innervation. There could though be an inhibitory adrenergic component functioning through β-receptors in the glands. Propranolol, which blocks β-receptor sites (Black, Crowther, Shanks, Smith & Dornhorst, 1964), however, did not reduce the inhibition.

The catecholamine inhibition is most probably due to these substances exerting a powerful vasoconstrictor action at this site (Langley & Uyeno, 1922), and the ability of phentolamine to reduce or prevent the inhibition indicates that a vasoconstrictor mechanism is responsible for the inhibition.

Dibenamine (Nickerson & Goodman, 1947) and phenoxybenzamine are irreversible antagonists of noradrenaline and adrenaline at the α receptor sites responsible for activation of vascular smooth muscle, and phenoxybenzamine is one of the most potent known antagonists at this site (Fellows,

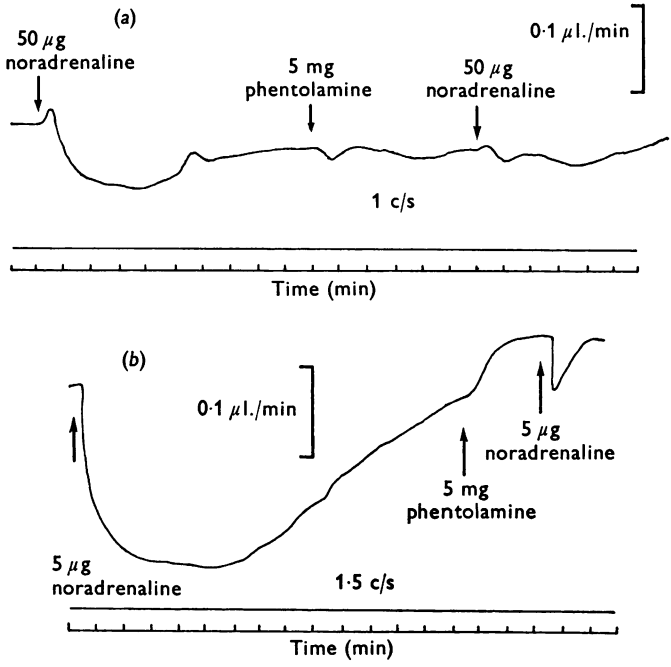

Fig. 7. Effect of phentolamine on the noradrenaline inhibition. (*a*) Effect of 5 mg intravenous phentolamine on the inhibition due to 50 μg intravenous noradrenaline. (*b*) Effect of 5 mg intravenous phentolamine on the inhibition due to 5 μg arterial noradrenaline. The pre-phentolamine noradrenaline administration was made 2 hr after the intravenous infusion of 17 mg/kg phenoxybenzamine.

McLean, Macko, Kerwin, Hall, Milnes, Witt & Ullyot, 1954). The onset of blocking action by these drugs is relatively slow. The inhibitory catecholamine effect was still pronounced, however, several hours after administering these blockers. The ineffectiveness of these drugs in preventing the catecholamine inhibition is difficult to explain.

The greater the activity of the glands when the noradrenaline or adrenaline were given the greater the inhibitory effects would appear to be. Thus at high frequencies of stimulation a marked inhibition always occurred, whilst at low frequencies the response was variable in its direction.

Resting glands are probably always activated by noradrenaline (as shown by Lloyd, 1959) or adrenaline, but the concomitant vasocon-

striction may not normally allow the activity of the glands to become great enough to enable the ducts to be filled with sweat and produce a secretion at the skin surface. Human eccrine sweat glands will readily respond to an initial intradermal injection of adrenaline or noradrenaline. Although the cat's pad gland cells themselves may be less receptive to noradrenaline or adrenaline stimulation, it seems more likely that the vasoconstrictor activity of these drugs has a greater effect in the cat's pad. Hence the acetylcholine or mecholyl response is more readily decreased by catecholamines in the cat than the human (K. G. Foster & J. S. Weiner, unpublished results). Either the vasoconstrictor action of these catecholamines is considerably greater in the pad than in the human skin or the metabolism of the cat's pad gland cells is less able to cope with the decreased oxygen supply resulting from this vasoconstriction.

In the human there is a decreased responsiveness to successive doses of adrenaline (Collins, Sargent & Weiner, 1959; K. G. Foster and J. S. Weiner, unpublished results). This effect was also evident in the cat's pad.

The transient increase in rate that often occurred when noradrenaline or adrenaline was given whilst the glands were actively secreting could be due to the direct stimulation of the secretory mechanism occurring before the onset of the vasoconstriction or due to expulsion of fluid in the ducts as a result of myoepithelial contraction.

Because of the overpowering inhibitory action of noradrenaline or adrenaline it is extremely unlikely that catecholamines released by the adrenal medulla in the cat can directly cause the glands to secrete.

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