shape of the dose-effect curve, and the lack of interaction with theophylline.

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Oxymetazoline-sensitive and -insensitive presynaptic α-adrenoreceptors in isolated rat atria

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Presynaptic α-adrenoreceptors have been found in many sympathetically-innervated tissues and their stimulation by released noradrenaline (NA) appears to play an important role in the regulation of the release of the neurotransmitter (Langer, 1977). However, α-adrenoreceptor agonists do not invariably decrease transmitter overflow in response to adrenergic nerve stimulation; see for example, McCullough, Rand & Story (1972).

Recent experiments in our laboratories suggest that there may be two populations of presynaptic α-adrenoreceptors in adrenergic nerves in rat atria; one being sensitive and the other being insensitive to oxymetazoline.

Isolated atria from adult male Wistar rats were superfused with McEwen's solution aerated with 95% O_2, 5% CO_2 at 37°C. Adrenergic nerves were stimulated, at supramaximal voltage using a pulse width of 0.5 ms for 15 s every 5 min at frequencies of 2–8 pulses/s, by placing two electrodes 3 mm apart in contact with the right atrium in the region of the sinuatrial node (Abbs & Elworthy, unpublished).

P values for frequency response curves were calculated using regression analysis.

Analysis of responses to adrenergic nerve stimulation indicated that atria could be divided into two groups (A & B). Increases in atrial rate and tritium overflow (in atria preincubated with [^{3}H]-NA) were greater at all stimulation frequencies in group A than in group B ($P < 0.001$, $n = 44$, d.f. = 168, atrial rate; mean tritium overflow (d min^{-1} $pulse^{-1}$) ±s.e. mean at 4 pulses/s group A = 39.5 ± 10.6, $n = 4$; group B = 16.3 ± 3.2, $n = 8$. $P < 0.05$). Atrial responses to NA were similar in both groups. Of 56 atria tested 28 were in group A and 28 in group B.

Oxymetazoline (10^{-10}–10^{-8} M) reduced atrial responses at all frequencies of adrenergic nerve stimulation in group A ($P < 0.001$, $n = 33$, d.f. = 124, 10^{-10} M). These atria were relatively insensitive to piperoxane (10^{-8} and 10^{-7} M); a significant increase in atrial responses to adrenergic nerve stimulation being observed only at 10^{-7} M ($P < 0.05$, $n = 10$, d.f. = 32).

Group B atria were insensitive to oxymetazoline, in the above doses, but piperoxane (10^{-8} and 10^{-7} M) increased atrial responses at all frequencies of adrenergic nerve stimulation ($P < 0.001$, $n = 13$, d.f. = 44, 10^{-8} M).

Atrial responses to NA were not affected by oxymetazoline or piperoxane in either group.

It is suggested that the presynaptic α-adrenoreceptors in group B atria may be subjected to maximal feedback inhibition from released endogenous NA and are thus unresponsive to oxymetazoline whereas in group A they are subjected to much less inhibition and are responsive to the drug.

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