adrenergic neurotransmission in the CNS as already reported in the peripheral nervous system (Starke & Altmann, 1973; Dubocovich, *et al.*, 1979). Medgett, McCulloch & Rand (1978) demonstrated that an increase in the concentration of NA in the synaptic gap may shift the effects of clonidine from agonist to antagonist activity on presynaptic alpha-adrenoceptors. The fact that DMI antagonizes the inhibitory effect of clonidine on central noradrenergic neurotransmission could be relevant to the attenuated hypotensive effect observed for this imidazoline when administered in association with some antidepressants in spontaneously hypertensive rats (Dadkar, Dohadwalla & Bhattacharya, 1978) and in man (Briant, Reid & Dollery, 1973).

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Inhibitory presynaptic effects of hydralazine on noradrenergic nerve terminals of the rat tail artery

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It has been shown previously that the effects of hydralazine (HYD) on arterial smooth muscle are modulated by the release of ATP and/or adenosine from sympathetic nerve terminals (Worcel, 1978; Worcel & Saïag, unpublished). Nerve released purines have been implicated in an inhibitory feedback regulation in sympathetic terminals (Verhaeghe, Vanhoutte & Shepherd, 1976; Enero & Saïdman, 1977). In consequence it appeared interesting to explore the possibility of the existence of a presynaptic interaction between HYD and purines.

The preparation used was the rat tail artery already described. In a first series of experiments we have studied the vasoconstrictor responses of the proximal segments of the artery induced by field stimulation. Indeed, we have observed that the contractile response of the proximal segments of innervated arteries from normotensive Wistar rats, induced by exogenous agonists (phenylephrine, serotonin, lysine-vasopressin) was practically not affected by concentrations of HYD as high as 1 μM (Worcel, 1978). Conversely, the contractions induced by field stimulation were sizeably inhibited by HYD (0.3 μM and 3 μM). In order to confirm the existence of an HYD presynaptic effect, we studied the actions of the drug on tritium efflux-stimulation induced (S.I) from arteries loaded with [^{3}H]-noradrenaline. Indeed, HYD caused an inhibition of the S.I tritium efflux, which reached a plateau effect very rapidly, after 5 min of HYD superfusion. The reduction of fractional release induced by HYD is dose-dependent. The threshold of this presynaptic response is low, 30 nM produces a 30% reduction of S.I efflux. The dose-effect curve for the inhibitory presynaptic effect is extended, the maximal action of HYD not being obtained at 3 μM.

We have observed that theophylline (0.5 mM) potentiates the postsynaptic (smooth muscle) effects of HYD (Worcel & Saïag, unpublished). Conversely, theophylline appears to be ineffective presynaptically since a concentration of 0.5 mM did not alter significantly the inhibitory effect of HYD on the S.I tritium efflux from the rat tail artery.

In conclusion, the present results indicate that HYD has in addition to its action on vascular smooth muscle, a very marked effect on sympathetic nerve terminals. Nonetheless, the mechanism of this presynaptic inhibition appears to be different from the postsynaptic effect, given the much shorter delay, the

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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