Pre-synaptic α-adrenoceptors and the inhibition by uptake blocking agents of the twitch response of the mouse vas deferens

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Field stimulation of the mouse vas deferens releases noradrenaline (Henderson, Hughes & Kosterlitz, 1972; Jenkins, Marshall & Nasmyth, 1975) and elicits a twitch response. Inhibition of neuronal uptake by cocaine potentiates the response of sympathetically innervated organs to electrical stimulation, especially at low rates of stimulation (< 1 Hz) (Iversen, 1973). The effect of uptake inhibitors in the mouse vas deferens has now been investigated.

The inhibition of noradrenaline uptake by cocaine, cocaine plus oestradiol, or phenoxybenzamine was measured in intact vasa deferentia. A single vas deferens was incubated with [7-^{3}H]-(−)-noradrenaline (10 ng/ml; specific activity 9.8 Ci/mmol) for 10 min, washed, homogenized and the catechols then adsorbed onto alumina. The tritium counts were taken to represent [^{3}H]-noradrenaline uptake and this was 28.53×10^5 d min^{-1} g^{-1} tissue controls. The addition of cocaine (10 μM) decreased this by 93%; cocaine (10 μM) plus oestradiol (3.7 μM) by 87%, and phenoxybenzamine (15 μM) by 89% ($P < 0.001$ for all 3 cases).

The effect of these drugs on the twitch response was examined. An isolated vas deferens was stimulated at 0.2 Hz, 256 mA and pulse widths of 0.25–2.0 ms. The addition of cocaine (10 μM) or cocaine (10 μM) plus oestradiol (3.7 μM) significantly inhibited the twitch at all pulse widths ($P < 0.05$). Conversely, phenoxybenzamine (15 μM) significantly potentiated the twitch at all pulse widths ($P < 0.001$).

The differing effect of these uptake inhibitors on the twitch may be related to the pre-synaptic α-adrenoceptor blocking activity of phenoxybenzamine, a property not shared by the other uptake inhibitors. Stimulation of these receptors by noradrenaline can inhibit the twitch response in the mouse vas deferens (Marshall, Nasmyth, Nicholl & Shepperson, this Meeting). To test this possibility yohimbine, a selective pre-synaptic α-receptor blocking agent (Starke, Borowski & Endo, 1975) was used. Yohimbine (3.2–128 nM) reversed the inhibition produced by cocaine plus oestradiol and the twitch was now potentiated.

These results suggest that, in the presence of cocaine and oestradiol, noradrenaline released by electrical stimulation of the mouse vas deferens inhibits the twitch response via a pre-synaptic α-adrenoceptor.

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Further evidence for dopaminoceptors in the vas deferens

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There are conflicting reports about the neurotransmitter role of noradrenaline (NA) in the vas deferens of most species because large doses of NA are required to elicit a contraction (Graham, Al Katib & Spriggs, 1968; Birmingham, 1970). In most studies contractions of the vas deferens are resistant to alpha-adrenoceptor antagonists except at very high concentrations (Ambache & Zar, 1971). These led Ambache & Zar (1971) to challenge the concept that NA acts as the motor neurotransmitter substance in the vas deferens.

However there is little or no study on the effect of dopamine (DA) on the vas deferens. Tayo (1977) reported that in the isolated vas deferens of the rat, DA