Dopamine inhibition of the twitch response of the mouse isolated vas deferens

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An inhibitory presynaptic dopamine receptor is present in the rat vas deferens (Tayo, 1977) but not in that of the guinea pig (Stjärne, 1975). To obtain more information on species differences, the possibility that a presynaptic dopamine receptor was present in the mouse vas deferens has been investigated.

Dopamine (0.3–100 μM) produced a dose-related inhibition of the twitch response (0.2 Hz, 2.0 ms pulse width) of the mouse isolated vas deferens (IC_{50} 4.50 ± 0.34 μM: mean ± s.e. mean). The dopamine receptor antagonists α-flupenthixol (100 nM) and pimozide (300 nM) did not alter the inhibitory effect of dopamine. However, yohimbine (10 nM), a selective presynaptic α-adrenoceptor antagonist in the mouse vas deferens (Marshall, Nasmyth, Nicholl & Shepperson, 1978) shifted the dopamine inhibition curve to the right.

The inhibition produced by dopamine (10 μM) was inversely proportional to the frequency of stimulation, falling from over 80% at 0.2 Hz to less than 20% at 16 Hz. This pattern is similar to that of presynaptic α-adrenoceptor agonists e.g. clonidine (Marshall *et al.*, 1978).

The effect of dopamine upon the overflow of [^{3}H]-noradrenaline was investigated in vasa preloaded with [7-^{3}H]-(−)-noradrenaline (sp. act. 7.5 Ci/mmol). [^{3}H]-noradrenaline released into the Krebs solution was separated from its [^{3}H]-metabolites (Graefe, Stefano & Langer, 1973). The control fractional noradrenaline release after stimulation (1.0 Hz, 2.0 ms, 120 s) was $1.22 \pm 0.06 \times 10^{-3}$ and this increased ($P<0.01$; t-test) to $7.19 \pm 0.80 \times 10^{-3}$ in the presence of dopamine (30 μM). Yohimbine (100 nM) did not alter the dopamine fractional noradrenaline release. The increased overflow of [^{3}H]-noradrenaline produced by dopamine was unaffected by halving the calcium concentration of the Krebs solution (to 1.25 mM) and was of similar magnitude in the absence of stimulation ($5.53 \pm 0.67 \times 10^{-3}$). In the presence of cocaine (40 μM), dopamine (30 μM) still increased the stimulated fractional release of noradrenaline ($P<0.05$) and it remained unaffected by yohimbine (100 nM).

It is concluded that the dopamine inhibition of the twitch response of the mouse vas deferens is mediated by presynaptic α-adrenoceptors and not via dopamine receptors. The dopamine inhibition may be either a direct action and/or indirect via displaced noradrenaline. The displacement of noradrenaline by dopamine was independent of stimulation and calcium ion concentration. These effects are similar to those of tyramine but unlike this drug the action of dopamine was not blocked by cocaine.

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Opiate tolerance and cross-tolerance in the mouse vas deferens

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Morphine inhibits motor transmission in the mouse vas deferens (Henderson, Hughes & Kosterlitz, 1972). This effect is antagonized by low concentrations of naloxone and therefore appears to be mediated by opiate receptors. The present work has compared the effects of two opiate agonists, morphine and levorphanol, in the isolated vas deferens from naive mice and from animals chronically exposed to morphine.

Vasa from naive mice were suspended in a magnesium-free Krebs solution. The electrically induced twitch response (0.2 Hz, 2.0 ms) was inhibited by morphine (IC_{50} 0.6 μM) and levorphanol (IC_{50} 0.03 μM). The inhibition produced by morphine (10 μM) and levorphanol (3 μM) decreased with increasing frequency of stimulation (0.2, 1.0, 5.0, 10 & 16 Hz). Halving the calcium ion concentration of the Krebs (to 1.25 mM) (or the addition of magnesium 1.2 mM) in-