The effect of exogenous noradrenaline on the overflow of [^{3}H]-noradrenaline from the mouse vas deferens

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Exogenous noradrenaline, acting via pre-synaptic α-adrenoceptors decreases the release of endogenous noradrenaline from adrenergic neurones (Langer, 1977). However, Farnebo & Malmfors (1971) reported that exogenous noradrenaline increased the basal and stimulated overflow of tritium from mouse vasa deferentia preloaded with [^{3}H]-noradrenaline. This problem has now been investigated using methods described previously (Marshall, Nasmyth & Shepperson, 1978).

Noradrenaline (3 μM) increased the fractional release of [^{3}H]-noradrenaline approximately five fold during stimulation at 1 Hz, and doubled the twitch response of the tissue. The increase in overflow was prolonged, remaining elevated 14 min after the exogenous noradrenaline had been washed from the organ bath. Yohimbine (128 nM), added to the organ bath two min before the exogenous noradrenaline did not alter the increase in [^{3}H]-noradrenaline overflow, which, therefore, was unlikely to be related to an effect on pre-synaptic α-adrenoceptors. In agreement with Farnebo & Malmfors (1971) noradrenaline increased the basal overflow of tritium. This was due to a rise in [^{3}H]-noradrenaline, [^{3}H]-DOPEG and [^{3}H]-DOMA overflows, with no change in the non-catechol metabolites. These increases could be due to competition between the unlabelled exogenous noradrenaline and [^{3}H]-noradrenaline for neuronal uptake and storage.

To investigate this hypothesis cocaine (10 μM) was added to the Krebs solution to prevent neuronal uptake. This procedure greatly reduced the rise in basal release of [^{3}H]-noradrenaline and [^{3}H]-metabolites produced by exogenous noradrenaline. In Krebs containing cocaine, exogenous noradrenaline (3 μM) reduced the fractional release of [^{3}H]-noradrenaline during stimulation from $4.74 \times 10^{-4} \pm 1.12$ (mean ± s.e. mean) to $0.85 \times 10^{-4} \pm 0.03$. The twitch response was inhibited by 74.7 ± 2.08%. Addition of yohimbine (128 nM) two min before the noradrenaline prevented both the decrease in [^{3}H]-noradrenaline overflow and the inhibition of the twitch response, showing both to be due to stimulation of pre-synaptic α-adrenoceptors. The exogenous noradrenaline did not alter the fractional release of tritium on stimulation, because the percentage of [^{3}H]-noradrenaline in the tritium overflow fell from 18.6 ± 3.17 to 8.0 ± 2.34 while that of DOPEG rose from 47.3 ± 1.88 to 64.8 ± 3.48. The same changes in the composition of the tritium overflow are produced by the selective pre-synaptic α-adrenoceptor agonist clonidine (Marshall *et al.*, 1978).

In conclusion, in the presence of an uptake blocking agent, noradrenaline stimulates pre-synaptic α-adrenoceptors to produce a decrease in the fractional release of [^{3}H]-noradrenaline. These results support the view that stimulation of pre-synaptic α-adrenoceptors produces a change in the composition of the tritium overflow from this tissue.

NBS is an M.R.C. student.

References

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