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Binding studies on alpha-adrenoceptors and muscarinic cholinoceptors in rat heart ventricle: effect of chemical sympathectomy

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Noradrenaline release in the peripheral nervous system is regulated through a negative feed-back mechanism mediated by presynaptic alpha-adrenoceptors. In addition a number of other presynaptic receptors including inhibitory muscarinic cholinoceptors have been described (Langer, 1977; Starke, 1977).

Rat heart ventricle possesses a rich noradrenergic innervation with mainly postsynaptic beta$_1$ adrenoceptors. Postsynaptic alpha-adrenoceptors mediating a positive ionotropic effect have also been reported (Wagner & Brodde, 1978).

In the present experiments the binding of two alpha-adrenoceptor ligands, [3H]-dihydroergocryptine ([3H]-DHE) and [3H]-WB 4101 (2-([2',6'-dimethoxy] phenoxyethylamine-methylbenzodioxan), and the muscarinic cholinoceptor ligand, [3H]-quinuclidinyl benzilate ([3H]-QNB), to rat heart ventricular membranes were studied in normal animals and animals in which the noradrenergic nerve terminals were destroyed with 6-hydroxydopamine (6-OHDA) pretreatment for two weeks.

The two adrenoceptor ligands, [3H]-DHE and [3H]-WB 4101, each bound with a single high affinity component with apparent dissociation constants (K_D) of 2.3 ± 3.0 nM and 2.0 ± 0.6 nM respectively. The maximal binding (Bmax) of [3H]-DHE and [3H]-WB were 374.2 ± 36.3 fmoles/g tissue and 275.7 ± 50.5 fmoles/g tissue respectively. Membranes prepared from sympathectomized animals showed decreases in maximal binding of 59.4% for [3H]-DHE ($P<0.002$) and 24.3% for [3H]-WB 4101 ($P<0.25$) when compared with those prepared from control animals.

The loss of alpha-adrenoceptor binding sites after sympathectomy suggests that some of these sites are located presynaptically on noradrenergic nerve terminals in the rat heart ventricle.

The muscarinic cholinoceptor ligand, [3H]-QNB, also showed high affinity, single component, binding with a Kd of 0.8 ± 0.1 nM and Bmax 646.2 ± 99.2 fmoles/g tissue. After 6-OHDA treatment the maximal binding was not significantly altered ($P>0.25$).

Our finding of unchanged muscarinic cholinoceptor binding after sympathectomy is in contrast to the recent report of Sharma & Banerjee (1978) who described a significant decrease in [3H]-QNB binding after 6-OHDA treatment. They interpreted their results as a loss of presynaptic cholinoceptors localized in noradrenergic nerve endings. The unchanged ([3H]-QNB binding seen in the present experiments suggests however that muscarinic cholinoceptors in the rat heart ventricle are localized mainly postsynaptically.

In summary the present results support a presynaptic location for alpha-adrenoceptors regulating noradrenaline release. Furthermore preliminary experiments have shown that the displacement of the alpha-adrenoceptor ligands from heart ventricle membranes by yohimbine and prazosine is different in normal and 6-OHDA treated animals.

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