

selectivity was not observed with orciprenaline. *In vivo* salbutamol and soterenol were many times more active than orciprenaline as bronchodilator agents when given intravenously, orally, or by aerosol. At effective bronchodilator doses salbutamol had less activity on the heart than soterenol. The selectivity shown by salbutamol and soterenol further substantiates the hypothesis of Lands & Brown (1964), who suggested that β -receptors can be divided into two distinct groups, β_1 and β_2 .

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Structure-activity studies on the *Helix* dopamine receptor

R. J. WALKER* and G. N. WOODRUFF (introduced by J. CROSSLAND), *Department of Physiology and Biochemistry, University of Southampton*

Walker, Woodruff, Glazner, Sedden & Kerkut (1968) studied the effects of α - and β -receptor blocking agents on the inhibition produced by dopamine in neurones of the *Helix* brain and concluded that the dopamine receptor in this preparation resembles the α -receptor for adrenaline.

The problem remains as to whether dopamine acts on the classical α -receptor or whether there are, in the *Helix* brain, specific dopamine receptors. The present investigation is concerned with a study of structure-activity requirements for dopamine-like activity in specific neurones of *Helix aspersa*.

The electrical activity was recorded from identifiable cells in the right parietal ganglion of the isolated snail brain, using methods similar to those previously described (Walker *et al.*, 1968). All the cells used in this study were hyperpolarized and inhibited by dopamine, applied by addition to the bath (0.005 to 0.025 μ -mole) or by iontophoretic injection (100 to 200 nA).

Five of the compounds tested showed dopamine-like activity and caused inhibition of cell firing rate. The potency of these compounds was expressed as the ratio of the molar doses of the compound and of dopamine required to produce the same period of inhibition. The most suitable dose of dopamine was usually 0.005 μ -moles. N-methyldopamine was equipotent with dopamine with a range of 0.5 to 2.2. 5-methoxydopamine and (-)-noradrenaline had mean equipotent molar ratios of 16.5 (range 8.5 to 34.0) and 17.3 (range 0.6 to 57.5) respectively. (+)- α -methyldopamine had a mean equipotent molar ratio of 30.7 (range 0.9 to 183.5) while (-)-adrenaline had a mean equipotent molar ratio of 91.8 (range 22.8 to 113.9). The number of observations ranged from seven to twelve for each compound.

The other compounds tested included isoprenaline, isoetharine, orciprenaline, (\pm)-octopamine, tyramine, (-)-metaraminol, (\pm)-oxedrine, hydroxyamphetamine, 3-methoxydopamine, *p*-methoxyphenylethylamine, apomorphine, 3,4-dimethoxyphenylethylamine and methoxamine. None of these compounds had any dopamine-like activity in doses of up to 1,000 times the effective dose of dopamine.

Using the technique of iontophoretic injection, the dose ratios, compared with dopamine, of N-methyldopamine, adrenaline and noradrenaline, were similar to those obtained by addition to the bath.

It is concluded that, in the neurones studied in this investigation, the receptor for dopamine resembles a true dopamine receptor rather than an α -adrenaline receptor.

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Dual effect of noradrenaline on incorporation of ^{32}P into phospholipids of rat brain

P. M. KEEN and J. M. SNEDDON*, *Department of Pharmacology, University of Bristol, Bristol BS8 1TD*

Noradrenaline (NA) is present in brain, where it possibly functions as a chemical transmitter or as a modifier of nervous function. Noradrenaline might change neuronal activity by an effect on membrane phospholipids; to test this possibility we have investigated the effect of NA on the incorporation of ^{32}P into phospholipids of rat brain *in vitro*.

Rat brain stems were homogenized (10% w/v) in sucrose-Tris-EDTA (0.25 M-10 mM-0.5 mM, pH 7.4). The homogenate was centrifuged at 1,000 g for 10 min, the

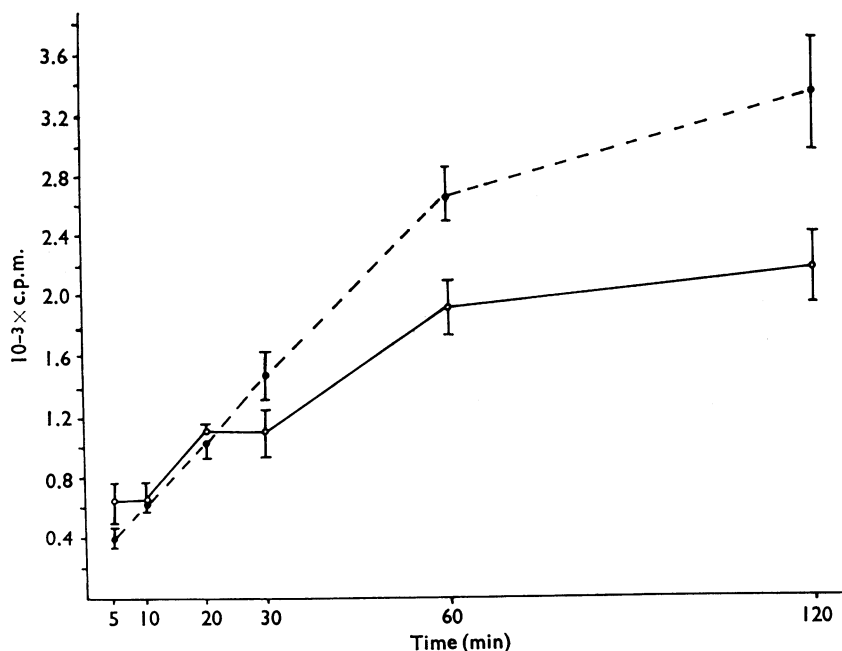


FIG. 1. Incorporation of ^{32}P into phospholipids of rat brain homogenates. ○—○, Control; ●---●, 5×10^{-6} g/ml. (—) noradrenaline bitartrate. Radioactivity expressed as ^{32}P incorporated into total phospholipids per mg homogenate protein. Vertical bars represent S.E. Means of five experiments.