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Evidence of central cardiovascular effects of intracerebroventricular isoprenaline in anaesthetized rat

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Isoprenaline (1, 2 and 4 μg) injected intracerebroventricularly in urethane anaesthetized rat produced a long lasting hypotension and tachycardia. It is unlikely that these effects are related to leakage in peripheral circulation of the amine because: (1) After intraventricular injection, [^{3}H]-isoprenaline diffused partially out of the central nervous system, but maximal blood and heart levels measured 5 min after administration were about 2 ng/g. These concentrations were unable to induce cardiovascular effects when injected intravenously. (2) In rats cephalic cross-circulation experiments indicated that intraventricular injection of 8 μg isoprenaline to the rat donor produced tachycardia which was not observed in the second animal.

The present study showed that isoprenaline had mainly central cardiovascular effects after intracerebroventricular injection.

Characteristics and altered sensitivity of cerebral β-adrenoceptors assessed by [^{3}H]-propranolol binding

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Studies on the nature and characteristics of the β-adrenoceptor have been greatly assisted by the observation that in many tissues this receptor is closely associated with the enzyme adenylate cyclase (Robison, Butcher & Sutherland, 1971). We have previously utilized this approach in assessing catecholamine-induced cyclic AMP formation in chick cerebral hemispheres and have provided evidence that these effects are mediated by a βadrenoceptor (Nahorski, Rogers, Smith & Anson, 1975). In the present study we have extended our experiments on the characterization of this receptor by examining the binding of ^{3}H propranolol, a specific ligand for the β-adrenoceptor (Nahorski, 1976), to chick cerebral membranes.

Experiments were performed on 1–6 day old male Ranger chicks. Cyclic AMP formation was determined in 0.37 mm incubated slices of the cerebral hemispheres by a protein binding assay. [^{3}H] (±)-propranolol binding was examined in a crude synaptic membrane fraction prepared by differential centrifugation (Nahorski, 1976). The order of potency of the catecholamines to stimulate cyclic AMP formation, isoprenaline > adrenaline > noradrenaline, was also observed in the ability of these compounds to displace [^{3}H]-propranolol from membrane binding sites. Salbutamol, although only a partial agonist, had a similar potency to adrenaline in both of these systems and dopamine was inactive at concentrations up to 100 μM.

(–)-Propranolol was a potent antagonist of isoprenaline (1 μM)-stimulated cyclic AMP formation ($IC_{50} = 7 \times 10^{-8}$ M) and [^{3}H]-propranolol binding ($IC_{50} = 1 \times 10^{-8}$M). (+)-Propranolol was about 100-fold less potent in both systems. H35/25(1-(*p*-tolyl)-2-isopropylamino-1-propanol), a relatively specific β_2-