medulla (from 0.440 ± 0.092 to 0.792 ± 0.100, $P < 0.05$, $n = 6$) and in the hypothalamus (from 0.168 ± 0.056 to 0.372 ± 0.072, $P < 0.05$, $n = 6$). In the hypothalamus, A increased from 0.05 ± 0.01 to 0.08 ± 0.01 μg/g wet wt. ($P < 0.05$, $n = 6$). No change was seen in noradrenaline or dopamine concentrations of medulla or hypothalamus. A single dexamethasone injection did not change PNMT after 24 hours. Five daily injections increased PNMT by 56%, but only in the medulla. Five daily injections of dexamethasone to newborn rats had no effect on PNMT in hypothalamus or medulla, but caused a 14-fold increase in PNMT and a 30-fold increase in A in the superior cervical ganglion.

These observations are consistent with the hypothesis that the cell bodies of PNMT and adrenaline containing neurones are present in the medulla and that they send axons to terminate in the hypothalamus. The PNMT contained in the cell bodies appears to be inducible by glucocorticoid hormone, and the induced enzyme is transported to the hypothalamus, resulting in an increased A content.

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Release of ^{3}H-(−)-noradrenaline from guinea-pig hypothalamic slices: effects of adrenoceptor agonists and antagonists

B.J. BRYANT*, M.W. McCULLOCH, M.J. RAND & D.F. STORY

Department of Pharmacology, University of Melbourne, Parkville, Victoria, 3052, Australia

The release of noradrenaline from peripheral adrenergic nerves in response to electrical stimulation is enhanced by α-adrenoceptor antagonists and reduced by α-adrenoceptor agonists. These effects have been attributed to the presence of α-adrenoceptors on the terminal axons through which transmitter release is inhibited. The present experiments were designed to investigate whether the release of noradrenaline from hypothalamic slices of the guinea-pig was similarly affected by drugs acting on α-adrenoceptors.

Slices of hypothalamus were incubated with ^{3}H-(−)-noradrenaline, then repeatedly washed with Krebs-Henseleit solution until the rate of efflux of tritium from the tissue had fallen to a low level (approx. 1 h): then, the residual tritium was present as ^{3}H-noradrenaline. Stimulation of the slice with biphasic pulses at 10 Hz for 30 s resulted in an increase in tritium efflux. With successive periods of stimulation at 30 min intervals, there was a steady decrease in stimulation-induced efflux.

The effects of drugs on resting and stimulation-induced effluxes of tritium were determined by adding them 19 min before the second period of stimulation. When α-adrenoceptor agonists were used, cocaine (100 μM) was present to prevent their uptake and the displacement of labelled noradrenaline.

Noradrenaline decreased stimulation-induced efflux in a concentration-dependent manner in the range 2-50 μM. Dopamine was approximately equipotent with noradrenaline; adrenaline was less potent, the threshold concentration being above 5 μM; isoprenaline had no significant effect in concentrations up to 50 μM.

Piperoxane (10 μM) increased stimulation-induced efflux, but phenoxybenzamine (10 μM) and phentolamine (10 μM) had no effect. However, phentolamine (5 μM) antagonized the effect of noradrenaline (20 μM) in reducing stimulation-induced efflux.

The findings suggest the presence in the hypothalamus of α-adrenoceptors through which stimulation-induced release of noradrenaline from stores in the tissue can be inhibited, but feed-back modulation of release by transmitter noradrenaline impinging on these receptors appears to be less important than in peripheral adrenergic neurones.

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