Cyclic nucleotides and central cardiovascular control in the cat

PATRICIA J. CLIPSHAM, T.C. HAMILTON, A.A.E. HUNT & R.H. POYSER

Beecham Pharmaceuticals, Research Division, Medicinal Research Centre, The Pinnacles, Harlow, Essex

Cyclic nucleotides have been proposed as the physiological second messenger for a number of hormones and neurotransmitters (Sutherland, Robison & Butcher, 1968), and Delbarre, Senon & Schmitt (1977) and Walland (1975, 1977), using anaesthetised cats, have suggested that cyclic adenosine 3'5'monophosphate (cAMP) is a mediator in the central control of blood pressure. We have further explored this hypothesis by administering cyclic nucleotides themselves, and drugs which can modify endogenous nucleotide levels, into the IIIrd brain ventricle of conscious cats.

Arterial pressure was recorded in conscious cats from an indwelling catheter in the thoracic aorta; heart rate was obtained from the blood pressure pulse. Cannulae were implanted both into the IIIrd brain ventricle (by stereotaxic means) and a jugular vein, for the administration of drugs.

Papaverine (300 μg and 1 mg) infused into the IIIrd ventricle, increased mean arterial pressure (MAP) by 20 ± 7 (mean ± s.e. mean) mmHg (5 cats) and 41 ± 10 mmHg (4 cats) respectively. In 3 cats aminophylline (300 and 600 μg) infused into the IIIrd ventricle, increased MAP by 17 ± 2 and 39 ± 7 mmHg, respectively. Infusion of db-c AMP (400 μg) into the IIIrd ventricle, raised MAP (48 ± 5 mmHg) in 3 cats whilst this dose of db-c GMP was ineffective. Maximum pressor responses to these drugs occurred 2 to 4 min after infusion started and declined to pre-dose levels 10 to 40 min later. Tachycardia, of shorter duration, accompanied these pressor effects.

Imidazole 4' acetic acid (IAA, 600 μg, a phosphodiesterase stimulant), infused into the IIIrd ventricle, lowered MAP by 19 ± 1 mmHg with a concomitant bradycardia (3 cats).

The responses to central administration of the various agents were not due to leakage into the periphery as their intravenous administration produced opposite effects.

Phentolamine (200 μg) or propranolol (300 μg) infused into the IIIrd ventricle, reduced the rise in MAP caused by papaverine (1 mg) into the IIIrd ventricle.

These results confirm that elevation of cyclic nucleotide levels in the brain is associated with pressor responses whilst their reduction by a phosphodiesterase stimulant produces the converse effect on blood pressure. That exogenously administered db-c AMP, but not db-c GMP, given centrally, mimicked the pressor responses to papaverine and aminophylline implicates c AMP rather than c GMP as the mediator of these responses. Reduction in the pressor response to papaverine by an α- or a β-adrenoceptor antagonist suggests that both α- and β-adrenoceptors are involved in the pressor response. These latter findings are similar to those reported for the pressor responses evoked by electrical stimulation of the posterior hypothalamus in the anaesthetised cat (Philippu, Roensberg & Przuntek, 1973; Philippu & Kittel, 1977) and by noradrenaline infused into the IIIrd ventricle in the conscious cat (Day, Poyser & Sempik, 1976). However, further studies are required to determine if these pressor responses are accompanied by changes in endogenous c AMP levels in the brain.

References

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