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The effects of cinanserin and phentolamine applied by microiontophoresis in the spinal cord

S. BARASI & M.H.T. ROBERTS*

Department of Physiology, University College, Cardiff

Recent studies have shown that conditioning stimulation of the nucleus raphes medianus in the Fluothane anaesthetized rat increases the amplitude of the monosynaptic reflex evoked by dorsal root stimulation (Barasi & Roberts, 1974a). Intravenous L-tryptophan increased the effects of raphe stimulation, indicating that raphe stimulation may activate a pathway releasing 5-hydroxytryptamine (5-HT). More recent studies (Barasi & Roberts, 1974b) have shown that 5-HT applied by microiontophoresis into the ventral horn of the spinal cord increased the amplitude of the motoneurone field potential evoked by antidromic stimulation of the ventral roots. Conditioning stimulation of the nucleus raphes also increased the amplitude of the antidromic field potential. Intravenous (3-4 mg/kg) or iontophoretic (20-100 nA for 5-30 min) applications of cinanserin prevented the effects of raphe stimulation. The specificity of the blocking action of cinanserin remained uncertain, however, particularly as it was noted that a slight increase in dose caused a profound reduction in the amplitude of the unconditioned field potential. We have used noradrenaline as a control agonist to determine the specificity of the action of cinanserin.

Noradrenaline applied with iontophoretic currents between 50 and 100 nA increased the amplitude of the antidromically evoked field potential. Its effects were similar to those of 5-HT but the latency and response duration were longer. We recorded responses to alternate applications of 5-HT and noradrenaline and then superimposed an application of either cinanserin or phentolamine (20-75 nA for 5-20 min). Although both antagonists were capable of blocking responses to both agonists, this occurred with the higher currents of application and was usually but not always accompanied by reduction of the baseline field potential amplitude. The effects of cinanserin on 5-HT were more rapid and longer lasting than its effects on noradrenaline in 11 studies and were similar in two studies. Phentolamine had a greater effect on noradrenaline responses in seven studies and had a similar effect on noradrenaline and 5-HT responses in three studies. Occasionally, a very narrow dose range was identified when the antagonist reduced responses to the agonist without affecting the control agonist responses.

The facilitatory effects of conditioning stimulation of nucleus raphes were recorded during application of the antagonists. It was found that these responses could also be blocked by application of either antagonist but on every occasion the time course of the blockade closely followed the time course of the blockade of 5-HT.

We conclude from these studies that phentolamine and cinanserin can be used to differentiate between responses to noradrenaline and 5-HT in the spinal cord. The results lend support to the postulate that responses of motoneurones to 5-HT and conditioning stimulation of raphe are pharmacologically similar and differ from responses to noradrenaline.

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