Actions and interactions of microiontophoretically applied morphine with transmitter substances on brain stem neurones

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Numerous attempts have been made to link the effects of morphine with its ability to interact with putative neurotransmitters in the brain (Clouet, 1971 ; Way & Shen, 1971 ; Weinstock, 1971).

We have used the microiontophoretic technique to investigate the effects of morphine and its interactions with acetylcholine (ACh), (−)-noradrenaline (NA) and 5-hydroxytryptamine (5-HT) when applied to spontaneously active single neurones in the brain stem. Experiments were performed on partially cerebellectomized rats, anaesthetized with urethane (1·2–1·8 g/kg).

Microiontophoretic applications of morphine (0·5–1·0% solutions at 10–30 nA) for periods of 0·5–10·5 min increased the firing rate of 33 and reduced that of 17 out of 76 neurones studied. Excitation by morphine was often very powerful ; relatively slow in its onset ; lasted throughout the period of application and began to decay immediately the drug was switched off. Reduction in neuronal firing by morphine was in general gradual and usually continued after the end of the application, so that recovery was often prolonged.

When several applications of morphine were made to the same neurone an increase in the latency of onset and a reduction in the magnitude of the excitatory response was often observed (10 out of 13 neurones). This phenomenon was never observed with neurones inhibited by morphine (6 neurones).

Prolonged application of morphine blocked excitation by ACh, NA or 5-HT, although occasionally potentiation of the excitatory effects of these compounds was observed. When excitation by one substance was blocked by morphine, the excitatory effect of another was often unaffected, suggesting that there may be some specificity in the antagonistic actions. On the other hand neither inhibition by ACh, NA or 5-HT, nor excitation by glutamate or DL-homocysteic acid was ever affected by morphine.

There appeared to be no correlation between the effects produced by morphine and those of either ACh, NA or 5-HT when these compounds were applied to the same neurone.

It appears that morphine has complex actions when applied iontophoretically to brain stem neurones. Both excitatory and inhibitory effects can be observed and the excitation may show acute tolerance after repeated application of morphine. The excitatory effects of ACh, NA or 5-HT can be antagonized and in some instances potentiated by morphine.

REFERENCES

CLOUET, D. H. (1971). The alteration of brain metabolism by narcotic analgesic drugs. In: *Handbook of Neurochemistry*, Vol. 6, ed. Lajtha, A., pp. 479–508. Plenum Press, New York.

WAY, E. L. & SHEN, F.-H. (1971). Catecholamines and 5-hydroxytryptamine. In: *Narcotic Drugs*, ed. Clouet, D. H. pp. 229–253. Plenum Press, New York.

WEINSTOCK, M. (1971). Acetylcholine and cholinesterase. In: *Narcotic Drugs*, ed. Clouet, D. H. pp. 254–261. Plenum Press, New York.

Amino acid antagonists and the depression of cuneate neurones by γ-aminobutyric acid (GABA) and glycine

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Evaluation of amino acid antagonists requires that both iontophoretic potency and specificity are tested. Previous experiments on cerebral cortical neurones indicated that