Effects of morphine and pentazocine on the turnover of noradrenaline and dopamine in various regions of the rat brain

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Numerous studies using a variety of species implicate brain catecholamines in the analgesic activity of morphine. Yet the ability of single doses of morphine to lower brain noradrenaline (NA) levels would appear to be a species dependent phenomenon. Thus in the case of the dog, cat, rabbit, rat and mouse, only in the cat and mouse is a reduction in brain NA content readily achieved by single doses of morphine (Way & Shen, 1971). Regarding the rat, while brain levels of NA and dopamine (DA) are unaltered by moderate doses of morphine, the feasibility of drug-induced changes in NA and DA turnover rates cannot be discounted and it has recently been reported that the acute administration of both morphine and pentazocine, while exerting no effect on steady state levels, increases the turnover of DA, but not NA, in the rat brain (Sugrue, 1972). This study extends these observations to the effects of both morphine and pentazocine on the turnover of NA and DA in various regions of the rat brain.

Male Sprague-Dawley rats weighing 200–250 g were used and tissue levels of NA and DA were determined fluorimetrically. Turnover rates were calculated by the method of Brodie *et al.* (1966) following blockade of synthesis by α-methyl-*p*-tyrosine.

The I.P. injection of morphine (20 mg/kg) and pentazocine (60 mg/kg), doses refer to free base, 1 h prior to sacrifice had no effect on steady state levels of DA in the corpus striatum. Regression analysis of the exponential decline in striatal DA levels following α-methyl-*p*-tyrosine administration revealed that both morphine and pentazocine significantly altered the regression coefficient, the turnover of DA in the corpus striatum being increased 27% and 19% by morphine and pentazocine respectively. The I.P. injection of naloxone (5 mg/kg) 15 min prior to morphine and pentazocine prevented the observed increases in DA turnover.

Both morphine and pentazocine had no effect either on hypothalamic NA steady state levels or on its turnover. Although morphine had no effect on medulla-pons NA steady state levels a drug-induced increase of 34% in turnover rate was observed and this effect was antagonized by naloxone. Pentazocine had no effect on medulla-pons NA steady state levels and, unlike morphine, elicited no change in turnover.

The results of this study reveal that both morphine and pentazocine, at the doses and time employed, increase the turnover of DA in the rat corpus striatum thus indicating a morphine- and pentazocine-induced increase in striatal DA neuronal activity. Whereas both morphine and pentazocine have no effect on NA turnover in the whole rat brain and in the hypothalamus, the findings in this study suggest a morphine-induced increase in NA neuronal activity in the medulla-pons. This ability is not possessed by pentazocine.

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