and noradrenaline both elicited transient, but very profound, tremor and reversal of ptosis in reserpinized mice.

Pretreatment of reserpinized mice with phentolamine (30 mg/kg) or phenoxybenzamine (30 mg/kg) partially blocked the thermogenic actions of orally administered desipramine, subcutaneously injected noradrenaline and adrenaline, and intraventricularly injected noradrenaline. Chlorpromazine-induced thermogenesis was unaffected by phentolamine or phenoxybenzamine.

Pretreatment of reserpinized mice with (±)-propranolol (30 mg/kg) completely abolished the thermogenic effects of orally administered desipramine and chlorpromazine, and subcutaneously injected noradrenaline and adrenaline. Thermogenesis induced by intraventricular injection of noradrenaline was blocked by low doses of (±)-propranolol but unaffected by high doses. (+)-Propranolol (30 mg/kg) partially blocked the thermogenic effects of chlorpromazine and adrenaline.

Orally administered desipramine (3 mg/kg) and chlorpromazine (30 mg/kg) were unable to elicit their usual thermogenic effects in reserpinized mice when the animals were pretreated with α-methyl-*p*-tyrosine (80 mg/kg I.P., 24, 18 and 4 h before the thermogenic drug), an inhibitor of tyrosine hydroxylase. The thermogenic responses to subcutaneous injections of noradrenaline (0·5 mg/kg) and adrenaline (0·5 mg/kg) were unaffected by α-methyl-*p*-tyrosine, and the thermogenic responses to L-dopa (500 mg/kg S.C.) and intraventricularly injected noradrenaline (0·5 mg/kg) were potentiated.

Pretreatment of reserpinized mice with diethyldithiocarbamate (400 mg/kg I.P.), an inhibitor of dopamine-β-hydroxylase, reduced the thermogenic effects of desipramine (3 mg/kg orally), chlorpromazine (30 mg/kg orally) and L-dopa (500 mg/kg S.C.). Diethyldithiocarbamate did not modify the thermogenic effects of subcutaneously injected noradrenaline (0·5 mg/kg) and adrenaline (0·5 mg/kg), and potentiated the thermogenesis induced by intraventricularly injected noradrenaline (0·5 mg/kg).

These results are consistent with the hypothesis that catecholamines are involved in the reversal of reserpine-induced hypothermia in mice by desipramine and chlorpromazine.

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Effects of acutely administered analgesic drugs on rat brain 5-hydroxytryptamine turnover

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There is evidence to implicate brain 5-hydroxytryptamine (5-HT) systems in the mode of action of morphine (Tenen, 1968; Samanin, Gumulka & Valzelli, 1970). Relevant to such a concept, an increase in rat brain 5-HT synthesis following

the acute administration of morphine has recently been reported (Yarbrough, Buxbaum & Sanders-Bush, 1971). The present studies were undertaken to determine first, if such an effect is shared by other acutely administered analgesics and, secondly, if pretreatment with the narcotic antagonist naloxone prevents the morphine-induced increase in rat brain 5-HT turnover.

Male Sprague-Dawley rats weighing 200–250 g were used and brain levels of 5-HT and 5-hydroxyindole acetic acid (5-HIAA) were assayed fluorometrically. Drug-induced changes in the increased brain levels of 5-HT and 5-HIAA following the administration of pargyline and probenecid respectively were used as an index of alteration in brain 5-HT turnover (Neff, Lin, Ngai & Costa, 1969).

The I.P. injection of morphine (20 mg/kg), methadone (10 mg/kg), pethidine (50 mg/kg) and pentazocine (60 mg/kg) doses expressed as free base, 1 h prior to sacrifice had no effect on rat brain 5-HT steady state levels. Pentazocine and methadone had no effect on the brain content of 5-HIAA but the levels were significantly increased by morphine. Conversely, a significant decrease in 5-HIAA levels was produced by pethidine. The increase in brain 5-HIAA content following probenecid administration was significantly increased by morphine. Further evidence of a drug-induced increase in 5-HT turnover was the finding that the increase in brain 5-HT content following pargyline administration was significantly augmented by morphine. Unlike the situation with morphine, rat brain 5-HT turnover was unaffected by methadone, pethidine and pentazocine as indicated by the lack of drug-induced alterations in either the increased 5-HT or 5-HIAA levels following pargyline or probenecid administration.

The ability of morphine to potentiate the increases in brain levels of both 5-HT and 5-HIAA following the injection of pargyline and probenecid was antagonized by pretreatment with naloxone (5 mg/kg).

The results of this study confirm the reported ability of acutely administered morphine to increase rat brain 5-HT turnover. Furthermore, the morphine-induced increase in 5-HT turnover is prevented by the specific narcotic antagonist naloxone. Finally, rat brain 5-HT turnover is unaltered by acutely administered methadone, pethidine and pentazocine.

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Desmethylimipramine and the hypotensive action of clonidine in the rabbit

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Clonidine reduces arterial pressure both when administered systemically and when introduced directly into the cisterna magna. It has been proposed that its hypo-