Short Communications

Action of Neuroleptics and Antidepressants on the Hypothermia Produced by Dopaminomimetics Apomorphine and Piribedil in Mice*

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With 1 Figure

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Summary

Neuroleptics, antidepressants and anticholinergics were compared in their action on the hypothermia produced by apomorphine (AP, 5.0 mg/kg i.p.) or piribedil (PRB, 100 mg/kg i.p.) in mice. Anticholinergics atropine, scopolamine and benactizine did not affect either hypothermia in contrast to neuroleptics and imipramine-like antidepressants which antagonized both hypothermias. Among neuroleptics studied the minimal effective doses (MED) antagonizing AP hypothermia (APH) ranged from 0.006 (trifluperidol) to 0.5 mg/kg (chlorpromazine), while MED antagonizing PRB hypothermia (PRBH) ranged from 0.05 (trifluperidol and perphenazine) to 2.0 mg/kg (haloperidol). Amongst antidepressants the MED ranged from 0.2 (desipramine) to 5.0 mg/kg (amitriptyline) in the case of APH, and ranged from 0.025 (desipramine) to 0.5 mg/kg (amitriptyline) in the case of PRBH, the potency correlated directly with the adrenopositive activity. The higher activity of neuroleptics in the case of APH, and the discrepancy between the order of their effectiveness in tests of APH and PRBH are discussed. The data confirm that the stimulation of the dopamine receptors results in hypothermia and are in accord with the postulated importance of the adrenergic link in the hypothermia produced by dopaminomimetics.

* The results were presented at the Fourth All-Union Meeting of Pharmacologists of USSR (Theses of Reports, Leningrad 1976, pp. 230—231, in Russian).
Introduction

Some reasons have been presented (Schelkunov, 1977) that there is the noradrenergic link in the apomorphine (AP) hypothermia (APH) in mice (Lapin and Samsonova, 1968) which is initiated by the stimulation of the dopamine receptors in the brain (Barnett et al., 1972; Fuxe and Sjögquist, 1972; Schelkunov, 1972). One additional fundamental fact is that intracerebroventricularly (i.c.v.) injected 6-hydroxydopamine (6-OH-DA), depending on dose, fully prevent or strongly antagonize hypothermias, produced by AP and other dopaminomimetic drugs (piribedil, bromocriptine, CM 29-712, L-DOPA and small doses of amphetamine), while pretreatment of mice with desipramine or similar drugs which protect only the noradrenergic (but the dopaminergic ones) neurons from the destructive action of 6-OH-DA counteracts the antihypothermic effect of 6-OH-DA and preserves the hypothermic effect of dopaminomimetics (Schelkunov, in press).

The characteristic feature of APH is that both neuroleptics and imipramine-like antidepressants counteract it, while anticholinergics are ineffective (Schelkunov, 1968 a, b). These data have been confirmed by Barnett et al. (1972), Fuxe and Sjögquist (1972), Maj et al. (1974). The effectiveness of antidepressants in the test of APH, correlated with their adrenopositive activity, was one of the reasons which suggested to us the noradrenergic involvement with APH (Schelkunov, 1977). It was of interest to compare quantitatively in this respect AP and another "direct" dopaminomimetic drug piribedil (PRB) (Corrodi et al., 1972). It has been shown in several papers (see Kapturkiewicz and Sowińska, 1977) that PRB produces hypothermia in mice and rats and that separate neuroleptics and also antidepressants (Kapturkiewicz and Sowińska, 1977) antagonize it in occasional fixed doses.

Materials and Methods

Experiments were performed on about 5000 albino mice of SHR strain (bred from Swiss) of either sex weighting 18—24 g. In any one experiment mice of the same sex were used and the weight range was within 4 grams. The ambient temperature was between 18 °C and 21 °C in various experiments, within experiment change not exceeding 1 °C. Hypothermia in mice was evoked by i.p. administration of 5 mg/kg of AP or 100 mg/kg of PRB. AP and PRB hypothermias were of about the same intensity (−4 °C to −6 °C) but significantly more prolonged with PRB (more than 4 hours, as compared with 0.5—1.0 hours in the case of AP). Neuroleptics,