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P 'psychosedative' 'thiepin' i.v. microiontophoresis methiothepin /Roche/ 'serotonin' /Sigma-Chem./ 'noradrenaline' /Regis/ 'phenothiazine' thioridazine /Sandoz/ 'sedative' di'benzodiazepine' clozapine 'chlorpromazine' /SK+F/ 'haloperidol' /McNeil/ etc. influence on 'electrophysiol,' neuron act. modification by 'amphetamine' 'physostigmine' etc. 'brain' raphe nucleus intact cf. lesion rat /XXVI/ /XXXII/

Eur.J.Pharmacol. 39, No.2, 341-55 /1976/

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Effect of Antipsychotic Drugs on the Firing of Dorsal Raphe Cells I. Role of Adrenergic System.

The effect of antipsychotic and adrenolytic drugs on the firing of dorsal raphe cells was studied in rat brain.

Methods

Midbrain raphe neurons of male albino rats (220-280 g) were monitored electrically and serotonin (Sigma-Chem.), l-norepinephrine (Regis) methiothepin (Roche), piperoxane (Rhone-Poulenc), thioridazine (Sandoz), chlorpromazine (SK+F), and sotalol (MJ1999, Mead-Johnson) were given by microiontophoresis. Some rats received intraventricular injections of 6-OH-dopamine (Regis) 30 min after 1 mg/kg chlorimipramine pretreatment. Other rats had lesions or transections in the reticular formation, locus coeruleus or midbrain/diencephalon border. p-Chlorophenylalanine (Regis) (400 mg/kg 24 hr before recording) and pimozide (McNeil) were given i.p. and RO4-4502 (Roche) (800 mg/kg 45 min before recording), LSD, l-amphetamine, d-amphetamine, apomorphine, physostigmine (Regis), clozapine and thioridazine (Sandoz) and haloperidol (McNeil) were administered i.v. prior to recording.

Results

Methiothepin (0.12 ± 0.01 mg/kg), clozapine (0.94 ± 0.18 mg/kg) and thioridazone (3.9 ± 0.8 mg/kg), administered i.v., inhibited the activity of serotonergic neurons in the dorsal raphe nucleus. However chlorpromazine (17.6 ± 2.9 mg/kg), haloperidol (9.6 ± 1.6 mg/kg) and pimozide (30 mg/kg i.p.) did not inhibit cell firing. The inhibitory potency of these agents on raphe activity correlated with central noradrenergic blocking efficacy. Piperoxane but not propranolol or MJ1999, given systemically, caused inhibition of raphe activity. All of these agents and norepinephrine exhibited relatively weak or variable effects when applied to the raphe neurons microiontophoretically while LSD and serotonin produced rapid inhibition. The depressant effects of antipsychotic drugs and piperoxane could be reversed equally by d- and l- amphetamine and abolished by destruction of adrenergic pathways in the central nervous system by chemical, mechanical or electrothermic lesions. Methiothepin and clozapine effects were unaffected by physostigmine, apomorphine, parachlorophenylalanine or RO4-4602. All drugs decreased heart rate and had various slight effects on B.P.

8 Fig. 2 Tab. 78 Ref. S43/AG/CTW

HEL 20.29/LEX .052 HEL / LSD

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