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Antagonism of reserpine-induced emesis in pigeons: a screening method for antidepressant activity

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1. Various antidepressant drugs and procedures have been studied against reserpine-induced emesis in pigeons.
2. Electroconvulsions, pentylenetetrazol and a non-hydrazide monoamine oxidase inhibitor (pargyline) block reserpine emesis.
3. It is suggested that reserpine-induced emesis in pigeons provides a simple and reliable method for studying anti-reserpine activity, and the compounds effective in antagonizing this emetic response are likely to have antidepressant property.

Several tests have been used to assess antidepressant activity: namely, the study of monoamine oxidase (MAO) inhibition, reserpine or tetrabenazine antagonism, anticonvulsant action and various behavioural techniques such as conditioned avoidance, food reinforcement and self-stimulation. It has been suggested that, of these, antagonism to various effects of reserpine is a more reliable test for antidepressant activity (Chen, 1964). Reserpine induces emesis in pigeons and this response has been described as a sensitive and reliable test for evaluating reserpine and reserpine-like activity (Earl, Winters & Schneider, 1955). The present investigation was undertaken to determine the suitability of antagonism of reserpine-induced emesis in pigeons as an indicator of possible antidepressant activity.

Methods

Eighty pigeons of either sex, weighing between 200 and 380 g, were used. Emesis was induced by injecting an emetic dose (0.5 mg/kg) of reserpine, as reported by Gupta & Dhawan (1960). During the period of observation the birds were kept individually in wire mesh cages and food and water were withdrawn. A bird was considered protected if it did not vomit during the observation period of 2 hr following administration of reserpine.

Electroconvulsions were induced by delivering a supramaximal current of 150 m-amp for 0.3 sec (more than 10 times the threshold strength) through corneal electrodes. The drugs used in the present study were reserpine (Serpasil), pentylenetetrazol (Cardiazol), crystalline insulin and pargyline hydrochloride, all dissolved in

normal saline except reserpine, which was supplied in a special solvent. The drugs were injected into a pectoral muscle except insulin, which was administered intraperitoneally.

Results

The results are summarized in Table 1. A single exposure to electroconvulsions reduced the 100% emetic response of reserpine to 60%. When the birds were subjected to electroconvulsions once daily for 4 consecutive days the emetic response to reserpine was completely blocked. Pentylenetetrazol (50 mg/kg) given 4 hr before reserpine challenge decreased the emetic response to 60%. In pigeons treated with pentylenetetrazol (50 mg/kg) for 2 days, reserpine produced only 30% emetic response. Insulin, on the other hand, was ineffective in protecting the birds against reserpine emesis even in doses up to 10,000 units/kg. Moreover, these doses of insulin produced no convulsions in the birds. Pargyline (20 mg/kg) reduced the reserpine emesis to 20%.

Discussion

Clinically effective antidepressants include iminodibenzyl compounds, MAO inhibitors, sympathomimetic amines and deanol. Other procedures such as electroconvulsive therapy, insulin shock and pentylenetetrazol convulsions have also been employed in the treatment of depressive states. A reliable test for antidepressant activity should be able to demonstrate the efficacy not only of different antidepressant drugs but also of these procedures. Reserpine-induced emesis in pigeons is effectively antagonized by iminodibenzyl compounds (imipramine, desmethylimipramine, amitriptyline and opipranol), hydrazide MAO inhibitors (pheniprazine and iproniazid), sympathomimetic amine (methamphetamine) and deanol (Gupta & Dhawan, 1960; Gupta, Saxena, Dhawan & Chandra, 1966). Pargyline, a non-hydrazide MAO inhibitor, also blocks reserpine-induced emesis in pigeons. Electroconvulsions and pentylenetetrazol are also effective in antagonizing the emetic response of reserpine. Thus, reserpine emesis in pigeons is antagonized by all the antidepressant

TABLE 1. *Effect of drugs/procedures on reserpine-induced emesis*

No. of pigeons	Drug/procedure	Dose/ parameters	Reserpine (0·5 mg/kg) challenge after	% emetic response
10	Control	—	—	100
10	Electroconvulsions	150 m-amp for 0·3 sec	4 hr	60
10	Electroconvulsions	150 m-amp for 0·3 sec for 4 days	4 hr*	0
10	Insulin	10,000 units/kg	3 hr	100
10	Insulin	10,000 units/kg	8 hr	100
10	Pentylenetetrazol	50 mg/kg	4 hr	60
10	Pentylenetetrazol	50 mg/kg for 2 days	4 hr*	30
10	Pargyline	20 mg/kg	1 hr	20

* After exposure to last procedure or drug.

drugs and procedures, the only exception being insulin. Very high doses of insulin neither produced convulsions nor protected the birds against reserpine emesis. Miller & Wurster (1956) also found that reptiles and birds are relatively resistant to the effects of insulin.

Actions of reserpine which have been used to study the antidepressant activity of drugs are ptosis (Maxwell & Palmer, 1961), hypothermia (Vernier, Hanson & Stone, 1962), adynamia (Sigg, 1962) and facilitation of seizures (Chen & Bohner, 1961). Reserpine hypothermia is antagonized by electroconvulsions (Jaju, Gupta & Dhawan, 1968), but there is a wide variation in response of animal body temperature to reserpine and the antidepressant drugs and animals are required in large numbers to establish a dose–effect relationship (Vernier *et al.*, 1962). Reserpine adynamia in rats is not antagonized by elecroconvulsions (Jaju *et al.*, 1968) and this limits its usefulness as a test for antidepressant activity. Antidepressant drugs antagonize the reserpine-induced facilitation of seizures, but this antagonism may not be specific for antidepressant drugs and is likely to be observed with any other general depressant. Chen (1964) suggested that antagonism of reserpine-induced ptosis in mice is the most satisfactory test for antidepressant activity because it is fairly specific and can also be quantitated (Rubin, Malone, Waugh & Burke, 1957), but we have observed that it is not antagonized by electroconvulsions (Jaju *et al.*, 1968). In contrast, reserpine emesis in pigeons is antagonized by electroconvulsions and its quantitation is easier and does not involve any subjective bias of the observer. Antagonism of reserpine-induced emesis in pigeons is not specific for antidepressant drugs; the response is blocked by a variety of substances including morphine, yohimbine and LSD-25. We consider, however, that it provides a simple and useful method for the assessment of possible antidepressant activity.

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