The Effect of Haloperidol, Spiperone and Pimozide on the Flexor Reflex of the Hind Limb of the Spinal Rat*

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Summary

It was found that spiperone and pimozide in doses which themselves do not influence the flexor reflex of the hind limb of the spinal rat inhibit stimulation of this reflex induced by serotoninomimetic drugs (LSD and fenfluramine). Higher doses of spiperone depress the flexor reflex and inhibit the stimulating effect of clonidine. Pimozide has no such effect. Haloperidol in doses which do not influence the action of LSD and fenfluramine produces a depression of the flexor reflex and antagonizes the action of clonidine. Our findings indicate that, irrespective of their antidopamine action, spiperone has a central antiserotonin effect and an antinoradrenaline one, pimozide—an antiserotonin one and haloperidol—an antinoradrenaline one.

Introduction

In our previous paper we observed that a number of neuroleptics, e.g. haloperidol, spiperone and pimozide antagonize the L-5-hydroxytryptophan (L-5-HTP)-induced behavioural syndrome in rats and mice (Maj et al., 1978). This fact seems to indicate that they have a central antiserotonin action. In other experiments we proved that the flexor reflex of the hind limb of the spinal rat is a good model for

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evaluation of the central antiserotonin activity (Maj et al., 1976). 5-Hydroxytryptamine (5-HT) antagonists, such as cyproheptadine, mianserin, danitracen and metergoline do not affect this reflex, yet they inhibit its stimulation evoked by 5-HT-mimetics e.g. tryptophan, L-5-HTP, LSD, fenfluramine, quipazine (Maj et al., 1976; Maj et al., in press; Palider et al., 1977). Therefore we decided to study the effect of haloperidol, spiperone and pimozide on the flexor reflex, using LSD and fenfluramine to induce serotonergic stimulation.

The preparation of the flexor reflex of the spinal rat makes it possible, at the same time, to find a noradrenolytic activity. In this case it is especially important since, on the one hand, the noradrenolytic activity has been observed in a number of neuroleptics (Janssen et al., 1965) and, on the other hand, typical noradrenolytics as phenoxybenzamine and phentolamine antagonize distinctly the L-5-HTP-induced behavioural syndrome (Maj et al., 1978). Therefore, we also assessed the examined neuroleptics with respect to their effect on noradrenaline (NA) neurons, although they had been already studied in this regard by other authors (Janssen et al., 1965).

Materials and Methods

We carried out the experiments on male Wistar rats, 170—230 g, using the technique previously described. A rat's paw was stimulated by means of an electric impulse, released from the stimulator every 1 min and a contraction of the musculus tibialis anterior was registered (Maj et al., 1976).

Clonidine, fenfluramine, LSD and haloperidol dissolved in 0.9 % NaCl, and spiperone—in 1.5 % aqueous solution of tartaric acid, were injected i.v. Pimozide, suspended in 1 % aqueous solution of Tween 80, was injected i.p. Haloperidol and spiperone were administered 1 hour before drugs stimulating the flexor reflex, while pimozide—4 hours before them.

Substances Used

Clonidine hydrochloride (Boehringer, Ingelheim), fenfluramine hydrochloride (Servier), haloperidol (Gedeon Richter), LSD (Delysid, Sandoz), pimozide (Janssen Pharmaceutica), spiperone (Janssen Pharmaceutica).

Results

The results are summarized in Table 1.