LETTER TO THE EDITOR

Toxic interaction between disulfiram and tranylcypromine stereoisomers in rats

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In the course of experiments to determine the role of central catecholamines on the effects of the stereoisomers of tranylcypromine (*trans*-(±)-2-phenylcyclopropylamine sulphate) on behaviour in rats, a toxic interaction was found between disulfiram and the stereoisomers.

Thirty male albino Wistar rats, 250–300 g, were housed in groups of 5 in 60 × 40 × 20 cm transparent cages in a thermostatically controlled room (23°) on a 12 h light-dark cycle (lights on 8 a.m. to 8 p.m.). They had free access to tap water and a wet mash diet for 3 weeks before treatment with drugs.

All five rats in a cage received the same treatment which was an intraperitoneal injection (5 ml kg^{-1}) of either sterile isotonic saline or disulfiram (300 mg kg^{-1}) dissolved in 0·4% carboxymethylcellulose administered at 10 a.m. followed at 11:30 am. by an intraperitoneal injection (2 ml kg^{-1}) of either the (+)- or (−)-isomer of tranylcypromine (10 mg kg^{-1}) or sterile isotonic saline (vehicle). Thereafter the behaviour of the rats was studied continuously.

Backward circling, tremor, vocalization, teeth chattering and convulsions began 15–30 min after administration of the (−)-isomer in rats pretreated with disulfiram. After about 1 h of convulsions and tremor, these rats became prostrate and died 2-4 h later. In contrast, the (−)-isomer in rats pretreated with saline caused no untoward effect.

Similarly, tremor, backward circling and convulsions appeared 30–60 min after administration of the (+)-isomer in rats pretreated with disulfiram. After about 2 h of tremor, circling and convulsions, these rats also became prostrate and died in 2–3 h. Administration of the (+)-isomer in rats pretreated with saline lead to tremor and backward circling, but convulsions, prostration and death did not occur.

None of the saline-treated rats pretreated with either disulfiram or saline showed any of the described effects.

Thus, the combination of disulfiram and either stereoisomer of tranylcypromine proved highly toxic in rats with the adverse effects of the combination of disulfiram and the (−)-isomer beginning sooner and being the more pronounced. But when administered alone in the doses used, neither drug was toxic.

Clinical trials indicate that the (−)-isomer may be an effective antidepressant agent (Escobar, Schiele & Zimmerman, 1974) while disulfiram is used to treat alcoholism (Goodman & Gilman, 1975), an illness which is often associated with depression. It is conceivable, therefore, that disulfiram and the (−)-isomer of tranylcypromine might be administered together to patients which might lead to severe toxic reactions.

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