Fenfluramine and body temperature

Fenfluramine is an anorectic drug structurally similar to amphetamine but devoid of central and cardiovascular stimulant properties in experimental animals and in men (Colmore & Moore, 1966; Le Douarec, Schmitt & Laubie, 1966; Ziance & Kinnard, 1968). The experiments here reported suggest, however, that fenfluramine may display stimulant properties in certain experimental conditions, such as the increased availability of catecholamines produced by dopa in monoamine oxidase inhibitor pretreated mice. (+)-Amphetamine sulphate, (±)-fenfluramine hydrochloride and S992 [trifluoromethylphenyl(benzoyloxy)ethylamino-2-propane], were tested in different experimental conditions according to the following schedule: Group 1: saline; group 2: pheniprazine (10 mg/kg i.p.); Group 3: L-dopa (25 mg./kg i.p.); Group 4: pheniprazine + L-dopa.

(+)-Amphetamine sulphate, 2 mg/kg, i.p., given to control mice did not affect the body temperature (Fig. 1B), while it was hyperthermic on increasing the dose to 5 mg/kg (Fig. 1C). Fenfluramine and S992 were never hyperthermic when given to control mice up to a dose of 30 mg/kg, i.p.

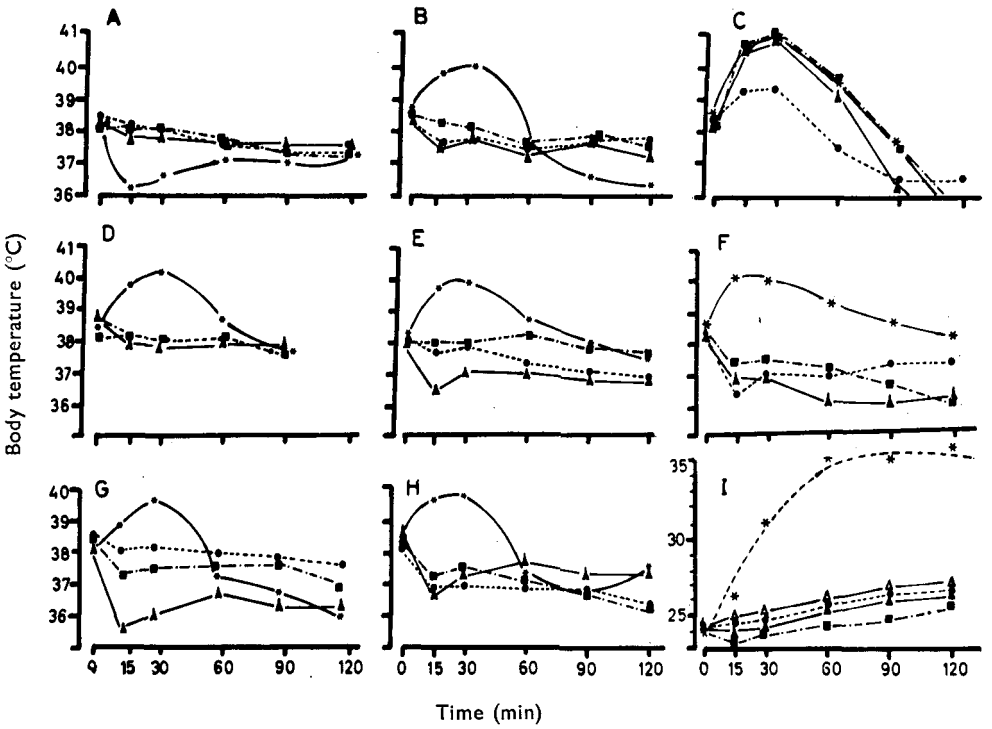

FIG. 1. A to H: Body temperature of groups of 5 mice receiving i.p. injections of: ●—● saline, ▲—▲ dopa, 25 mg/kg, ■-·-·-■ pheniprazine, 10 mg/kg, ★—★ pheniprazine + dopa. Except group A, in all other figures, beside this treatment, mice received i.p. amphetamine, fenfluramine or S992 at the doses listed below. Pheniprazine was given 16 h before the test. Fifteen min after the tested drugs, L-dopa was given and body temperature recorded 15, 30, 60, 90 and 120 min later. A. Saline. B. Amphetamine 2 mg/kg. C. Amphetamine 5 mg/kg. D. Fenfluramine 7·5 mg/kg. E. Fenfluramine 15 mg/kg. F. Fenfluramine 30 mg/kg. G. S992 15 mg/kg. H. S992 30 mg/kg.

I: Indicates the body temperature of mice injected i.p. with 5 mg/kg of reserpine 16 h before the test. △—△ saline, ★- - - - -★ amphetamine, 5 mg/kg, ▲—▲ fenfluramine 15 mg/kg, ●- - - - -● fenfluramine 30 mg/kg, ■-·-·-■ S992 15 mg/kg.

From Fig. 1A it can be seen that L-dopa displays a mild hypothermic action in monoamine oxidase-blocked mice. This hypothermia is reversed to a clear hyperthermia not only by amphetamine but also by fenfluramine and S992 at any dose studied. The hyperthermia was accompanied by clear signs of excitation. From a more detailed examination it appears that amphetamine (2 mg/kg) and fenfluramine (7·5 mg/kg) act similarly in all the four experimental conditions (Fig. 1B and 1D). At higher doses (Fig. 1C, E, F) the picture is different. Amphetamine itself elicits hyperthermia, which is further increased by L-dopa or pheniprazine. On the contrary, fenfluramine alone produces hypothermia which is unaffected by L-dopa or pheniprazine.

In comparison with the above conditions, where catecholamine levels are increased, the effect of fenfluramine on body temperature was tested on mice made hypothermic by reserpine. After reserpine, amphetamine increases the body temperature while fenfluramine and S992 fail to modify it (Fig. 1 I).

These studies show that the effect of fenfluramine and its derivative may differ from or be similar to amphetamine according to the availability of catecholamines. Also Le Douarec & others (1966) concluded, on the basis of different experiments, that fenfluramine may show both sedative and stimulant effects at the same time.

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BOOK REVIEW

ISOLATION AND IDENTIFICATION OF DRUGS in pharmaceuticals, body fluids and post-mortem material. Edited by E. G. C. Clarke assisted by Judith Berle. Pp. xxii + 870 (including index). The Pharmaceutical Press, London, 1969. £14.

Isolation and Identification of Drugs is, as is claimed in the descriptive brochures, an entirely new book which should fill a gap which has long been apparent in the literature of human toxicology. This book has been produced as a companion volume to the Extra Pharmacopoeia and indeed there is a marked resemblance in size and style. It is offered as a practical manual and data book for forensic scientists, toxicologists, analytical chemists, pharmacists, biochemists, pathologists and police surgeons; whilst of undoubted value to the former groups the value to police surgeons must be limited. Since it is a companion volume to the Extra Pharmacopoeia, it is perhaps unfortunate that the habit encountered in the toxicological literature of intermixing data for mice (rats, guinea-pigs etc.) and men has been allowed to invade the present volume. However, Professor Clarke and his team of collaborators and assistants have succeeded admirably in their task and are to be congratulated on the production of a volume which has been in almost constant use (in at least one laboratory) since its publication.

The concept of this work is ambitious in that an attempt has been made to provide details of methods and techniques for the identification of many drugs under condi-