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Amphetamine toxity in aggressive mice

SIR,—The toxic effects of amphetamine in mice can be influenced by a number of factors: weight of the animal (Chance, 1947; Fink & Larson, 1962), environmental temperature (Hohn & Lasagna, 1960; Askew, 1961; Fink & Larson, 1962) noise (Chance, 1946, 1947; Cohen & Lal, 1964), the number of animals in a cage (Chance, 1946; Burn & Hobbs, 1957) and painful stimuli (Weiss, Laties & Blanton, 1961).

Mice kept isolated for a long time and showing aggressiveness also show increased sensitivity to the toxic effects of amphetamine.

Male, Swiss, albino mice, weighing about 20 g were used. They were kept usually 6/cage in Makrolon cages with a floor surface of 40 cm^2 at a room temperature of 22° and a relative humidity of 60%.

Aggressive mice were obtained (Yen, Stanger & Millman, 1959) by isolating the animals in individual cages of the same dimensions, but with an opaque wall, for four weeks. After this period, the mice became aggressive and fought amongst themselves when they were grouped.

Dexamphetamine was given intraperitoneally in different doses to both normal and aggressive mice. Each group contained isolated and grouped animals. The toxicity was calculated after 24 hr (Litchfield & Wilcoxon, 1949).

The results are in Table 1.

TABLE 1. TOXICITY OF AMPHETAMINE IN NORMAL AND AGGRESSIVE MICE

Experimental condition	LD50 (and 95% confidence fiducial limits) of dexamphetamine in mg/kg/i.p.	
Normal mice		
— isolated	47·5	(32·7 — 68·8)
— grouped	9·0	(8·0 — 12·0)
Aggressive mice		
— isolated	11·0	(7·3 — 16·5)
— grouped	3·7	(2·6 — 5·3)

A minimum of 48 mice was used for each experimental group.

The toxicity of dexamphetamine is increased in aggressive mice compared with normal mice whether they are isolated or grouped at the moment of the administration of the drug.

Since Halpern, Drudi-Baracco & Bessirard (1962) suggested a correlation between amphetamine toxicity and the level of brain catecholamines, this was investigated, but when brain 5-hydroxytryptamine and noradrenaline was

determined spectrofluorometrically (Shore, 1959) these were the same for normal and aggressive mice.

Our results add another factor to the many already known to affect amphetamine toxicity. They also provide a new lead to the understanding of biological changes occurring during the development of the aggressive behaviour.

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A method for evaluating imipramine-like agents in rats*

SIR,—Demonstration of imipramine-like activity in animals is difficult. Stein & Seifter (1961) reported that the increase in self-stimulation rate induced by methamphetamine was enhanced by imipramine as a result of augmentation of the central adrenergic reward system. We have now investigated the behavioural effects of amphetamine and imipramine in animals trained for an automatic pole-climbing apparatus (Aceto, Kinnard & Buckley, 1963).

A group of six male albino rats (250–350 g) was trained to climb a pole in response to an auditory signal, and so avoid a shock delivered by an electrified grid floor. A successful climb depressed a microswitch which terminated the trial and permitted a longer intertrial period. The apparatus was programmed so that 100 trials could be presented during a 2 hr session. Each trial consisted of 8 sec of auditory tone (avoidance phase), 6 sec of auditory tone plus shock (escape phase) and 58 sec of intertrial time. A shock scanning device was used which energized the grid by scanning at the rate of 3 times/sec. Current was measured by ammeter, and rats were shocked with 500 V at about 3 mA.

Animals were trained to avoid shock in 95% or better of the trials. In the experiments reported here, none of the drug-treatments significantly impaired the ability of the rats to successfully avoid or escape. The avoidance response latency for each rat was recorded by means of a pen polygraph; 16 control days revealed that the rats climbed the pole in an average time of 5·4 sec, with a range of 4·9 to 6·0 sec. Salts of the drugs, imipramine (hydrochloride) and amphetamine (sulphate), were injected intraperitoneally in saline once a week

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