this series. Further work is in progress and details will be published elsewhere.

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PHARMACOLOGY

Effect of Monoamine Oxidase Inhibitors on the Behaviour of Rats in Hall's Open Field

ALTHOUGH numerous methods are available for assessing the potency of monoamine oxidase inhibitors *in vivo*, these almost invariably rely either on the direct measurement of tissue levels of catecholamine, serotonin or some metabolite thereof[1], or on the ability of the inhibitor to potentiate or nullify the effects of some other drug such as 5-hydroxytryptophan, tryptamine or reserpine[2]. Direct behavioural effects of monoamine oxidase inhibitors at low doses are usually slight or detectable only by use of conditioned response techniques[3].

In a series of aralkylhydrazines we have noticed a correlation between the monoamide oxidase inhibitory powers of these compounds and their effectiveness in producing changes in the behaviour of normal untrained rats in Hall's open field[4]. Individual rats were placed for a period of 3 min. in an open drum 6 ft. in diam. with 2 ft. high walls. The floor of the drum was divided into foot squares. The number of times the rat preened, reared and defæcated were counted as well as the number of fæcal boluses passed and the number of squares traversed.

The results are shown in Table 1.

Inhibition by monoamine oxidase *in vitro* was measured by incubating various concentrations of the inhibitor with guinea pig liver mitochondria for 15 min. at *p*H 7·4 and 25°. Tyramine was then added and the residual monoamine oxidase was assayed by the dinitrophenylhydrazine method[5]. The concentration giving 50 per cent inhibition (I_{50}) was determined by interpolation. In the experiments in column (*a*) semi-carbazide, which is required in the assay, was present together with the enzyme and inhibitor; in those in column (*b*) semicarbazide was added with the tyramine. Although there are some quantitative differences in the results obtained by these two different procedures, the general order of activity was not greatly affected.

The doses of drug producing behavioural changes are of the same order as those required to counteract the sedative effects of reserpine. The effects observed with the aralkylhydrazines persisted at least 24 hr., consistent with the very slow recovery of the inhibited enzyme[6]. The effects with harmine were much shorter (< 3 hr.), harmine inhibition of monoamine oxidase being readily reversible[7].

The relationship of the behavioural changes to the anti-depressant action of monoamine oxidase inhibitors is not clear, particularly as different aspects of behaviour were affected at the minimal effective dose with different compounds. It is, however, interesting to compare these results with those obtained with tranquillizers such as chlorpromazine where all aspects of behaviour studied in the open field were depressed. This effect has also been reported by Ryall[8].

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Table 1

Compound*	Approx. minimal effective dose (mgm./kgm.)† producing significant change from control behaviour (Groups of 8 rats)	Type of behavioural change at minimal effective dose	I_{50} (μmoles/l.) for monoamine oxidase inhibition *in vitro* (*a*)	(*b*)
p-Chlorobenzylhydrazine	2	Decrease in emotional defæcation	0·07	0·25
Benzylhydrazine	2	Decrease in emotional defæcation	0·2	0·4
3,4-Dichlorobenzylhydrazine	2	Decrease in no. of squares traversed and no. of times rearing	0·1	1·0
o-Chlorobenzylhydrazine	5	Decrease in emotional defæcation	0·25	0·2
3-Picolylhydrazine	10	Decrease in no. of squares traversed	1·3	1·3
4-Picolylhydrazine	>10	—	2·5	2·0
3,4-Dimethoxybenzylhydrazine	>10	—	2·5	1·2
α-Naphthylmethylhydrazine	>10	—	4·0	4·0
O-Benzylhydroxylamine	>20	—	>1,000	>1,000
Harmine	4	Decrease in no. of squares traversed	Not tested	0·5

* Hydrazines used as hydrochloride salts
† Drug given subcutaneously 3 hr. before test (except for harmine when it was 1½ hr.)

Variations in Inorganic Pyrophosphatase and Glutaminase in the Liver and Brain of Mice poisoned by Carbon Tetrachloride

J. HAGEN[1] has shown that carbon tetrachloride poisoning in factory workers induces extensive biochemical and metabolic changes in the central nervous system, liver and kidneys. On investigating the action of carbon tetrachloride in mice, Frunder