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The Action of Inhibitors of Catechol-O-Methyl-Transferase on the Exploratory Activity of Mice

SIR,—In a previous note we reported that pyrogallol enhanced inhibitory learning in rats (Izquierdo, I. and Merlo, 1963), and we considered it likely that this effect was due to a central adrenergic mechanism.

Using an actograph we have studied the exploratory activity in 77 white mice of 12 to 30 g. weight, before and after intraperitoneal injections of pyrogallol (3, 6, 12·5, 50 and 200 mg./kg.) and of 3,4-dihydroxyphenylacetamide (300 mg./kg.). The drugs were dissolved in 0·1 ml./kg. of distilled water just before injection. Control animals were given the water only.

The actographic records were run for 10 min. before, and for 20 min. after the injections. Only the definite suppression of exploratory activity was considered an inhibition. Responses were evaluated as the number of mice showing suppression at each dose of the drugs.

300 mg./kg. of 3,4-dihydroxyphenylacetamide suppressed exploratory activity of 9 out of 10 mice in which it was tested. The results obtained with pyrogallol are plotted in Fig. 1, in which the ordinates correspond to percentage of mice

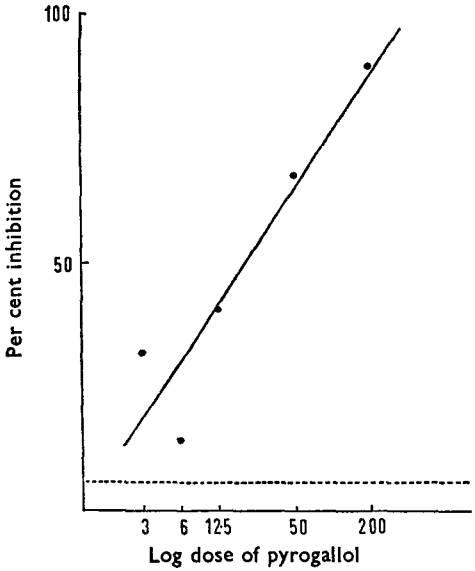

FIG. 1. Inhibition of exploratory activity of mice after pyrogallol. The broken line is the control response.

responding with inhibition, and the abscissae to the doses of pyrogallol in a logarithmic scale. The horizontal broken line corresponds to inhibitions seen in control animals.

Our results seem not to be due to just a non-specific motor impairment: 200 mg./kg. of pyrogallol had no effect upon a rota-rod test performed in 12 mice.

If the decrease of exploratory activity is taken as a measure of habituation (disappearance of the orienting reflex to a new environment), then these results are in agreement with those previously reported in which pyrogallol enhanced habituation as well as extinction in rats (Izquierdo, I. and Merlo, 1963). As both pyrogallol (Axelrod, 1960) and 3,4-dihydroxyphenylacetamide (Carlsson, Lindqvist, Fila-Hromadko and Corrodi, 1962) are inhibitors of catechol-*O*-methyl-transferase, and thereby increase the contents of catecholamines in various encephalic structures (Izquierdo, J. A., Jofre and Dezza, 1963 and unpublished), our data lend further support to the hypothesis of an adrenergic mechanism in the brain, related to inhibition.

ALICIA B. MERLO
IVAN IZQUIERDO*

Catedra de Farmacologia Experimental,
Universidad de Buenos-Aires.
Junin 956.
Buenos-Aires, Argentina.
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* Present address: U.C.L.A. Dept. Anatomy. Los Angeles 24, Calif., U.S.A.
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