Effects of diethyldithiocarbamate on the conditioned avoidance response of the rat

SIR,—Sodium diethyldithiocarbamate, the active metabolite of disulfiram, is a potent inhibitor of dopamine-β-hydroxylase *in vitro* (Goldstein, Anagnoste & others, 1964; Collins, 1965) and *in vivo* (Carlsson, Lindqvist & others, 1966). A single injection of the metabolite causes a decrease in brain noradrenaline content and a relatively small increase in brain dopamine. Compounds which effect the metabolism and distribution of catecholamines in brain such as reserpine, dopa and α-methyltyrosine also effect the maintenance of a conditioned avoidance response (Seiden & Carlsson, 1963, 1964; Moore, 1966), and evidence has been presented that the maintenance of a conditioned avoidance response requires dopamine or noradrenaline, or both (Seiden & Peterson, 1968). We have now measured the effects of diethyldithiocarbamate on the conditioned avoidance response.

TABLE 1. EFFECTS OF SODIUM DIETHYLDITHIOCARBAMATE ON CONDITIONED AVOIDANCE RESPONSES IN GROUPS OF 4 RATS

Dose mg/kg s.c.		Mean ± s.e. (%) responses at hr after injection			
		Normal	6 hr	24 hr	48 hr
125	(% avoid)	90·0 ± 1·8	92·5 ± 2·8	97·5 ± 2·2	96·2 ± 1·1
	(escape failure)	0	0	0	0
	(latency)	6·2 ± 0·9	6·5 ± 0·8	4·9 ± 0·5	5·3 ± 0·3
250	(% avoid)	95·0 ± 1·8	47·5 ± 13·3*	96·2 ± 1·1	96·2 ± 2·0
	(escape failure)	0	15 ± 11·6	0	0
	(latency)	5·7 ± 0·9	14·8 ± 3·6*	5·7 ± 0·5	5·4 ± 1·0
500	(% avoid)	96·2 ± 1·1	18·8 ± 7·2*	78·8 ± 18·4	96·2 ± 2·0
	(escape failure)	0	38·8 ± 20·4	11·2 ± 9·6	0
	(latency)	5·6 ± 0·6	21·8 ± 3·0*	10·0 ± 4·3	5·8 ± 0·6

* $P < 0.05$ Willcoxon Rank Test.

Male, albino rats (Holtzman Sprague-Dawley, 280–320 g) were conditioned (Seiden & Carlsson, 1963) in two modular testing units (12 in × 8 in × 7½ in) placed end to end, with an opening between them (4 in × 4 in). The conditioned stimulus was a buzzer; the unconditioned stimulus was an intermittent electrical shock delivered through a scrambler to the grid floor of the chamber (current 0·5 mA, duration 0·5 sec, frequency 1/2·5 sec). The conditioned-unconditioned stimulus interval was 15 sec. During training and testing, three types of responses were scored: if the rat crossed in response to the conditioned stimulus alone, an "avoidance response" was scored; if the cross occurred during the time when both the conditioned and unconditioned responses were being presented, an "escape response" was scored; if the rat failed to cross after receiving 6 shocks, an "escape failure" was scored. The latency is defined as the time (sec), required for the cross to occur. Forty trials were given to each rat daily (inter-trial time 45 sec) until a criterion of at least 90% avoidance responding was reached in the first or second block of 20 trials. When this occurred, an additional 20 trials were given the next day (overtraining session). Sodium diethyldithiocarbamate was injected 6 hr before testing, on the day after overtraining.

The performance of the conditioned avoidance response of rats 6 hr after treatment with 125 mg/kg of diethyldithiocarbamate did not differ significantly from their pre-injection performance. However, rats injected with either 250 mg/kg or 500 mg/kg showed depression of avoidance responding (50 and

80%, respectively) as well as an increase in the latency of the response (160 and 290%, respectively). At 24 and 48 hr after diethyldithiocarbamate injection no effects on the conditioned avoidance response were observed (Table 1).

Since the metabolite causes depletion of brain noradrenaline, it is possible that the effects of diethyldithiocarbamate on the conditioned avoidance response may be due to its effect on this catecholamine; however, it also has effects on other copper-containing enzymes, and has been shown to be a copper chelator (Frieden, 1962). Further work is necessary to establish a preference between the alternatives.

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Performance of the Ferranti-Shirley viscometer with automatic flow curve recorder unit

SIR,—A common method of investigating the rheological properties of materials which exhibit time dependent flow characteristics such as thixotropy is to use a rotational viscometer of, for example, the cone and plate type (see e.g. Boylan 1966, Talman, Davies & Rowan, 1967, Barry & Shotton, 1967). The Ferranti-Shirley viscometer (McKennell 1954, 1956, 1960, Van Wazer, Lyons & others, 1963) is designed so that when used in its automatic mode it is intended that the cone is accelerated at a uniform rate up to a preset maximum speed and then decelerated to zero speed at the same rate. A plot of torque on the cone against speed of the cone may then be displayed as a hysteresis loop on an X-Y plotter. This loop is then used to characterize the rheological properties of the system (Green, 1949, Green & Weltmann, 1946, Weltmann, 1960).

We have made a simple test on our instrument to check if acceleration and deceleration were constant (Barry, 1967). The sweep time was set at 600 sec, the indicator unit was switched to "check speed" and the maximum rev/min to 100, and the cone was set revolving; at the same time a stop watch (0·1 sec divisions) was started. The time was noted at every ten divisions of the speed scale and thus the time required for each increment of 10 rev/min obtained. The results are shown in Table 1.

Similar results were obtained using an alternative procedure. The cone rev/min was displayed as the Y coordinate on the X-Y plotter and the distance moved by the pen up this axis in equal increments of time (60 sec) was measured. Similar results were obtained with the same limits of reproducibility.