

Effects of Reserpine and Chlorpromazine on Nest Building and Thermal Preference in Rats. (22007)

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Reserpine and chlorpromazine have somewhat similar effects on animal behavior. Both drugs depress general activity(1,2) and reduce responsiveness to environmental stimuli(3-6). Both drugs also tend to cause hypothermia (1,4,8). This study attempted to determine whether two forms of basically unlearned motor behavior related to low temperature could be influenced by moderate amounts of these drugs. Hypothermia resulting from drug treatment might be expected to cause preference for a warm environment and increased nest building in rats; but general sedation, if marked, would tend to depress both nest building and active search for the preferred thermal environment.

Methods. Twenty-four male albino rats of Wistar stock, 120-180 days old and 275 g average weight were used. Thermal preference was measured in an apparatus consisting of 2 interconnecting plywood units (5 x 5 x 32 in.) in which the temperatures could be independently regulated by means of strip heaters(7). The temperatures were set at 14-18°C (room temperature), and 32-36°C, alternated each day with respect to unit heated. Illumination was provided by an overhead light. Each animal was given a daily test in the apparatus lasting 4 minutes. Every 10 seconds during the last 3 minutes of the period a notation was made of the unit in which the animal appeared. Preference was measured in terms of the frequency with which the animal appeared in the warmer unit. Thus a score from 0-18 was possible. Animals were maintained in large nesting cages (24 x 18 x 12 in.) with food and water always available. Nesting material was provided in the form of 150 g of wood shavings and 50 g of paper stripping. Each evening previous nests were broken up and the nesting material scattered

throughout the cage. On the following morning the nests were rated independently by the experimenter and a second person, using the scale of Stone and Walker(9). Ratings range from 0 for no evidence of a nest to 5.0 for an excellent nest. Room temperature was reduced to 10-14°C during the night to promote nesting and raised to 25°C between nesting periods. The first part of the experiment was a pre-drug phase of 4 days. Groups of animals equated on a basis of nesting performance were then assigned to the experimental treatments indicated in Table I. During this phase, subcutaneous injections of the drugs were given one hour before start of the nesting period. Reserpine was given as .25% solution in a propylene glycol base, chlorpromazine as 2% solution in isotonic saline.

Results. The results for nesting and thermal preference are shown in Fig. 1. The data were treated by 2-way analyses of variance in which effects of each drug and their possible interactions could be segregated. Pre-drug data showed no statistically significant group differences but thermal preference behavior was selective in that all animals preferred the cooler unit.

As shown by Fig. 1, reserpine affected both thermal preference and nesting behavior much more strongly than chlorpromazine. On the 3rd and 4th days of reserpine treatment (groups R and ChR) nest building was effectively abolished ($p < .001$) and a reversed preference for the warmer environment was established ($.05 > p > .02$; significance of mean frequency above expected chance frequency of 9). Chlorpromazine (groups Ch and ChR) inhibited nesting following the first and second injections. After the second day the apparent slight depression of nesting was of doubtful statistical significance ($p = .05$). Chlorpromazine alone had no effect on thermal preference. Disturbed thermal preference was evident for several days after discontinuing res-

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TABLE I. Experimental Groups.

Group	N	Treatment	Dose
R	6	Reserpine	.5 mg/kg for 3 days; .25 mg/kg on 4th day
ChR	6*	Chlorpromazine	10 mg/kg for 4 days
		Reserpine	.5 mg/kg for 3 days; .25 mg/kg on 4th day
Ch	6	Chlorpromazine	10 mg/kg for 6 days; 15 mg/kg for 2 days
C	6	Isotonic saline	Comparable volumes to group Ch

* All data discarded for one animal that died after first inj.; data for a second animal that died on 5th day was included in the analyses.

serpine but nest building recovered within one day.

Weight changes during nesting periods were also measured. Declines in weight, presumably reflecting reduced food intake, accompanied the depressed nesting. Prompt recov-

ery of weight followed discontinuance of reserpine injections.

Discussion. Both reserpine and chlorpromazine affected nesting behavior and weight loss but, with the doses used, the effects of reserpine were clearly much greater. Reserpine

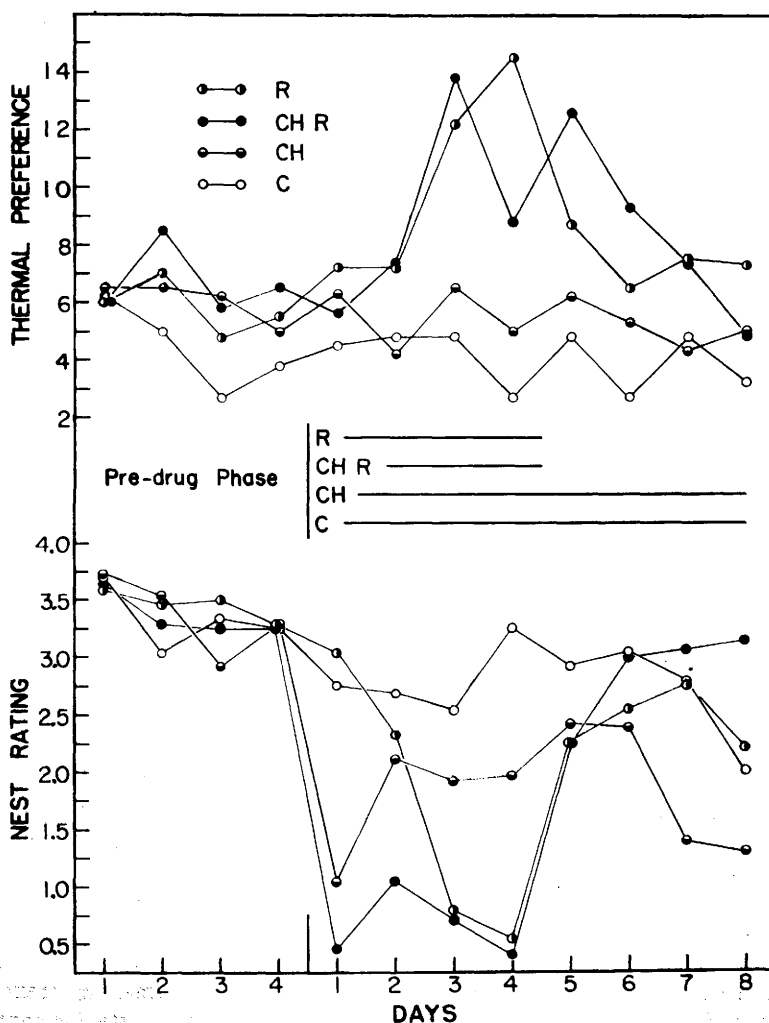


FIG. 1. Mean thermal preference scores and nest ratings.

alone affected thermal preference. Slight indications of synergic effects of the 2 drugs were seen but not statistically verified. The persistence of preference for a warmer environment for several days after discontinuing reserpine injections might be due to a persistent drug effect or to a persistence of a behavior learned during the drug phase.

It is of interest that reserpine greatly depressed one adaptive behavioral reaction (nest building) to the hypothermic state presumably resulting from the doses used but promoted another (choice of a warm environment). This difference may be related to the marked differences in the nature of the behavioral responses tested and the methods of testing. The thermal preference test involved arousal of the animal by handling, which could be expected to last throughout the 4-minute test period; nest building required long persistent activity under conditions of minimal disturbance. Reserpine-treated animals were easily aroused and quite active while awake but readily fell into a deep sleep when not disturbed. The experiment does not exclude, however, the possibility of a differential drug effect on mediational mechanisms of the two behaviors. The implications for behavioral research with reserpine in terms of distinguishing between sedative effects of the drug and other more specific actions are apparent.

Summary. Effects of reserpine, chlorpromazine and combined drugs on nest building and thermal preference of rats are described. In the doses used, reserpine alone had a marked and persistent effect on these functions. It depressed nest building while promoting choice of a warm environment. The differential behavioral effect is thought to be related to the great differences in persistence of activity required for the two tests and the ability of reserpine-treated animals to maintain alertness for brief periods after handling.

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Total Plasma Ascorbic Acid as Index of Stress in the Rat. (22008)

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One of the manifestations of physiologic stress is an increase in the production by the adenohipophysis of adrenocorticotrophin (ACTH) (1). A temporary rise in the concentration of total plasma ascorbic acid and plasma ascorbic acid following administration of ACTH in man has been reported (2).

As a preliminary to further experiments, it was deemed desirable to compare the sensitivity of this index of stress and possible ACTH titer in the blood of albino rats with

other such indices.

Methods. Animals in one group were anesthetized with sodium-ethyl-methyl-butyl-barbiturate (Nembutal) for 2 hours. Those in Group 2 were anesthetized with Nembutal for 2 hours and during this time non-activated electrodes were kept in contact with the left cervical sympathetic trunk just posterior to the superior cervical ganglion. The third group was treated like Group 2 except that the electrodes were activated so that the sym-