The Effect of Chlorpromazine on the Learning Process

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Introduction

The tranquilizer chlorpromazine apparently affects the brain by inhibiting the activities of the hypothalamus. When an animal is threatened or under stress, it responds with a number of physiological changes triggered by mechanisms within the hypothalamus, particularly in its posterior section. In this portion of the brain are centers which play an important role in the animal's automatic protective behavior. In the rear section is a system which controls emergency responses that prepare the animal for fight or flight.

When stimulated properly, nerve impulses are transmitted from the site of stimulation to the thalamus by means of pathways called lemnisci. From there the impulses are relayed to a section of the cerebral cortex which interprets the sensation. Parallel to the lemnisci is a system known as the activating system; located in the central core of the brain, it collects some of the impulses passing through the lemnisci and carries them directly to the midbrain reticular formation behind the hypothalamus. The reticular formation then in turn relays the impulses to the hypothalamus. From there, as when from the lemnisci, the impulses are sent to the cerebral cortex by way of the diffuse projection system. When stimulated, the activating system produces an arousal reaction. Work by Himwick (4) shows chlorpromazine in small doses blocks this reaction. Using an electroencephalogram it is possible to show a painful stimulus normally produces a great brain wave change which is indicative of arousal reaction; but while under the influence of chlorpromazine, no such brain wave change is produced upon administration of a painful stimulus. The impulses appear slowed and to some degree halted by the action of a tranquilizer, not passing above the hypothalamus into the cerebral cortex for interpretation.

DeRopp (1) and Southwick (5) agree that in substantial doses chlorpromazine may produce large reductions in blood pressures, tremors, gastric disturbances, skin eruptions, and possibly jaundice. It typically reduces basal metabolism and quiets agitated emotions.

According to Lashley (3), experiments with rats wherein lesions to the cerebral cortex involved an average of 28.4 per cent of area, indicated that the cerebral destruction produced no significant effect upon the learning ability of a particular habit.

At the present time there is conflicting evidence as to whether tranquilizers produce or induce an ill effect on the cerebral cortex or any brain area during the process of stimuli transportation and interpretation. This research was conducted to determine the effect of chlorpromazine on the learning process in white rats.

Methods

Two sets of trials were run, using different rats in the separate sets. In the first set of trials, shock avoidance was used in testing. A

modified Skinner box, or problem box, was separated in the center by a partition, making a square on each side of the partition with linear dimensions of 7″ x 7″, the entire base of which was a grid conducting the shock impulses. Two holes 2″ x 2″, separated from one another by 2½″, were cut in the partition, and one was marked in black for visual identification. Since one side of the Skinner box was of clear plastic and the other of opaque fiberboard, the sides were reversed for some of the trials, with no significant change in the rat's preference for the marked door. Four rats were used, two for controls and two as experi-

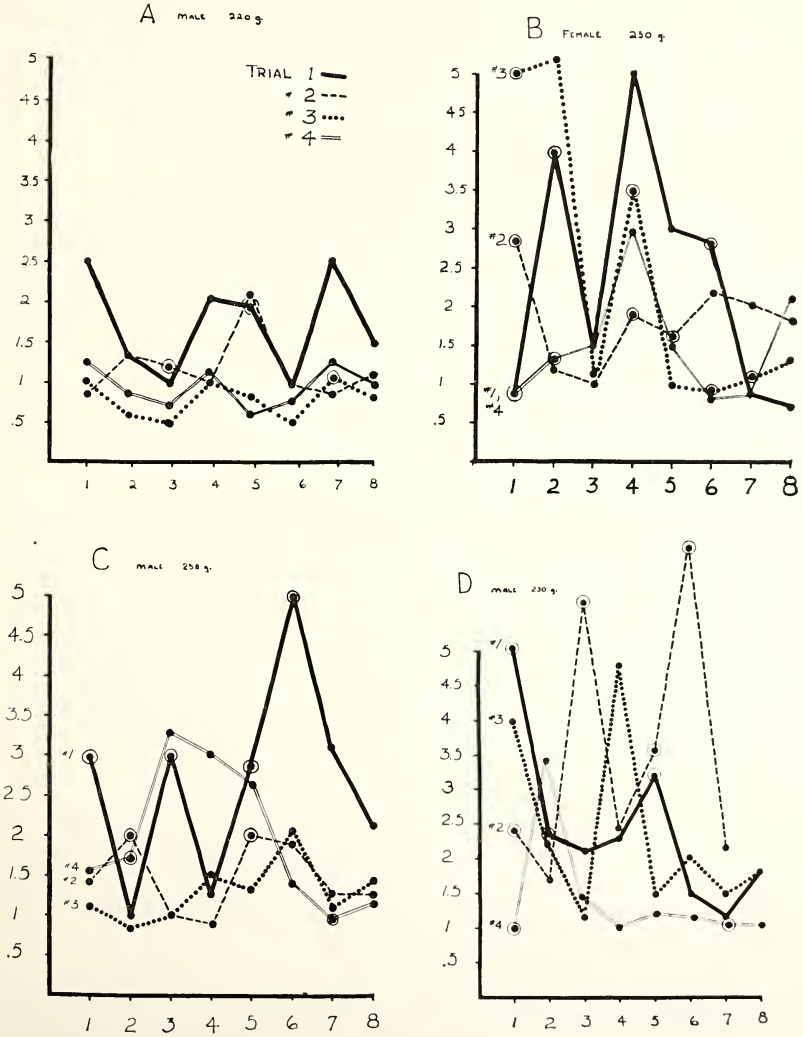

Figure 1.

mentals. The experimentals were chosen on the basis of earlier trials without the tranquilizer. For the experimentals, chlorpromazine was injected intraperitoneally approximately fifteen minutes before testing began. The tranquilizer was administered to the rats in the amount of .25 cc/50g. body weight. Fifteen minutes later, a rat was placed on one side of the partition facing away from the two holes. The shock and a timer were turned on simultaneously. If the rat passed through the marked hole, it was counted as a positive reaction and the shock was turned off immediately. If he passed through the unmarked hole, the reaction was counted as negative, and, while the time was turned off when the rat passed through the hole, the shock was left on for an additional two seconds. The same method was used on the controls with no tranquilizer. The times were entered to the nearest tenth of a second, with an indication of which were positive and which were negative. On the days of testing, a minimum of two trials per rat per day were run, with six to eight repetitions each trial.

Results

The results of the first set of experiments are shown in Figure 1. Rats A and B are the controls, and rats C and D the experimentals. Each circle around a particular time identifies a negative trial. The capriciousness of the only female rat tested may have been due partially to her pregnant condition. The extreme erratic behavior in the first two trials of rat D is noteworthy. Rat D was, when not under the influence of the tranquilizer, of very ill temper. In comparing the trials of individual rats against each other, the learning which occurred is apparent. Although not all of the rats showed progress as steady as rat A's, they appeared to be showing definite preference toward the correct hole. There is also an improvement in times as well.

Methods

In the second set of trials a runway was used in testing four female and three male rats who were on a twenty-three hour starvation diet. The runway was three feet long with a goal box at each end. The tranquilizer was administered as in the other trial. Each rat was placed in the end box without food with the door closed. A stop watch was started as the door was opened and stopped when the rat got all four feet into the goal box at the other end which contained some pellets of food.

Results

The results of the runway experiment are shown in Figure 2. Rats A, B, C, and D were the females; E, F, and G the males. The first nine trials were without the tranquilizer and the last five were with the tranquilizer. In all but G, the times of the tranquilized trials were slower than the control trials.

Discussion

For comparison between the controls and experimentals in the first set of trials, use of rats A and C would be best. While rat C took longer to adjust to the situation, his times dropped, especially in trial three,

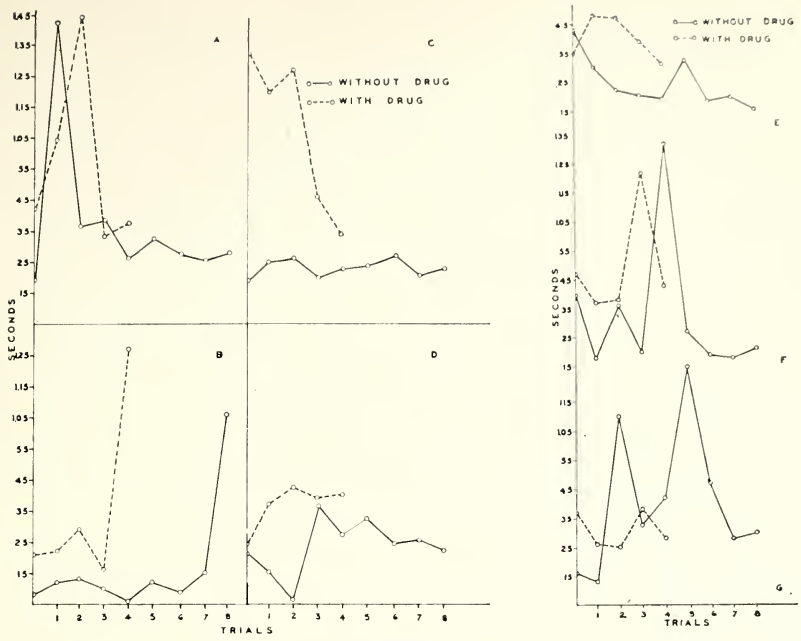

Figure 2

nearly to the level of rat A's. The inconsistency in rats B and D may have been due to the condition of B and the disposition of D.

Miller from Garattini (2), feels shock avoidance is the best method of testing because the apathetic conditions produced by a tranquilizer rule out the use of such drives as hunger and thirst. Electric shock can be used for motivation in almost any type of behavior. However, any emotional disturbance produced by the shock becomes an unwanted variable. In this experiment it became evident that it was easy to intensify the shock beyond that point which was safe and workable in rats, especially with the comparatively slowed reactions of the tranquilized rats. In reference to the second set of trials, the rats showed a fear of the device used for testing. Under the effects of the tranquilizer this fear was not so apparent. After the injection of the tranquilizer, the food consumption dropped in the experimentals. Their intake of water during the next twenty-three hours was also reduced.

Of the two sets of trials those using the Skinner box were more effective. The tests using the runway and the same rats for tests with and without the tranquilizer merely would test retention of the problem and not learning of a new situation.

It is difficult to determine whether the learning which was apparent in both experimentals and controls but definitely retarded in the experimentals was slowed because of a hindrance to the learning process or because of the relaxant and apathetic effects produced by chlorpromazine.

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