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EFFECT OF STELAZINE ON AVOIDANCE
LEARNING AND RELEARNING

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Ralph R. Swarr

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ABSTRACT

EFFECT OF STELAZINE ON AVOIDANCE LEARNING AND RELEARNING

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The effects of the tranquilizing drug, stelazine, on avoidance learning and relearning were examined in the present study. Five groups of rats were given 25 avoidance training runs in a modified Mower-Miller shuttle box, and an additional 25 trial runs were given 48 hours later in the same apparatus. It was found that there was significantly less avoidance learning among subjects which received 0.25 mg/kg of stelazine than among control animals, but the drugged rats were able to make the escape response. When subjects had a 0.25 mg/kg dosage during the initial learning session, an effect occurred which caused a reduction of relearning in the later trials when the animals were not drugged. The normal improvement of avoidance learning in the relearning trials over the level obtained in the initial training was inhibited by stelazine, but the compound did not cause avoidance to drop below a level which had been achieved in the first 25 trials.

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R. R. S.

TABLE OF CONTENTS

CHAPTER	Page
I. INTRODUCTION	1
II. METHOD	10
III. RESULTS.	14
IV. DISCUSSION	20
V. SUMMARY	23
REFERENCES	24

LIST OF TABLES

TABLE	Page
1. Summary of Studentized t Ratios of Group-Session Means Based on the Number of Avoidance Responses	15
2. Summary of t Values Based on the Mean Difference Between the Number of Avoidance Responses in Session I and Session II for Each Subject.	16
A-1.* Summary of Avoidance Responses for Subjects in All Groups for Session I and Session II . . .	27
A-2. Summary of Avoidance Response Data	28
B-3.* Summary of t Ratios of Group-Session Means Based on the Response Latencies of All Subjects	30
B-4. Summary of t Values Based on the Average Difference Between the Mean Response Latencies in Session I and Session II for Each Subject	31
B-5. Summary of Mean Latencies for Subjects in All Groups for Session I and Session II	32
C-6.* Comparison of Mean Avoidance with Mean Latencies for $\bar{S}$ s in All Groups for Session I and Session II	34

* "A, " "B, " "C" indicate the tables are in the Appendices.

LIST OF FIGURES

FIGURE	Page
1. Distribution of Culminative Mean Avoidance Responses from All Groups in Session I and Session II	17
2. Distribution of the Improvement of the Mean Total Avoidance Responses of Session II Over Session I for Each Group	19

LIST OF APPENDICES

APPENDIX	Page
A. Summary of Avoidance Response Data	26
B. Summary of Latency Data.	29
C. Comparison of Avoidance and Latency Data .	33

I. INTRODUCTION

Avoidance learning is learning a response following the onset of the CS which allows the subject to evade or prevent the occurrence of the noxious stimulus (US). It is assumed that fear or anxiety is an important mediator of avoidance. When the organism fails to avoid and receives the aversive US, the behavior which allows the animal to terminate the US is called escape behavior. Tranquilizing drugs have been used to determine if they would affect the animal's ability to learn avoidance as well as escape. The rationale of such studies develops from the hypothesis that if tranquilizers bring about reduction of fear in S, then the incidence of avoidance will be reduced.

This type of experiment has been conducted by researchers interested in contributing quantitative, behavioral data on the pharmacological profiles of tranquilizing compounds and by researchers seeking to identify some of the variables relating to the avoidance learning situation.

Tranquilization is a non-specific term referring to a number of compounds with varying chemical structures and pharmacological properties. Pharmacological effects generally assumed to result from the introduction of tranquilizing agents into an organism include such conditions as relaxation without anesthetic features (4, 12, 13), good motor coordination, and ability to be easily aroused (11). Berger (1) has divided the tranquilizing agents into the following groups according to similarity of chemical structure: Phenothiazine derivatives-- chlorpromazine hydrochloride, promazine hydrochloride, triflupromazine hydrochloride, mepazine, prochlorperazine, perhenazine, trimeprazine,

diethazine, ethopropazine, promethazine, pyrathiazine and stelazine; Rauwolfia alkaloids and fractions--rauwolfia serpentina, reserpine, rescinnamine, alseroxylon, and recanescine; Substituted propanediols--meproamate, phenaglycodal, and mephenesin; Diphenylmethane derivatives--benactyzine hydrochloride, and hydroxyzine hydrochloride; and the Ureide and Oxanamide--ectylurea and oxanamide. Brady (3) reviewed comparative behavioral pharmacological research and noted the necessity for more systematic, quantitative studies designed to determine the specific behavioral changes associated with the tranquilizing agents. Brady cited conditioned avoidance and other fear-type response patterns as the beginnings of reliable and operationally definable affective behavioral assay techniques.

In studying the effects of tranquilizing agents on conditioned avoidance behavior, investigators have utilized various techniques to distinguish those responses which were assumed to be mediated by emotional factors such as fear or anxiety. Compounds most frequently investigated from the three main groups (in terms of chemical structure) have been the Phenothiazine derivative--chlorpromazine, the Rauwolfia alkaloid--reserpine, and the Substituted propanediol--meproamate.

Cook and Weidley (5) utilized a pole-climbing apparatus to test the effect of chlorpromazine (and other drugs) on an avoidance learning response. Their one-foot square testing chamber had a grid floor which could be electrically charged, a buzzer mounted on the side, and a rough wooden pole (three-fourths inch in diameter) suspended from the ceiling. Pre-training trials consisted of a series of shocks (US), at the rate of five per second, which were delivered concurrently with the activation of the buzzer (CS) and continued for 30 seconds or until the S terminated the stimuli by climbing the pole (safety area). Following initial random behavior during the trials, the animals soon learned to climb the pole, and after 10 to 15 such sessions an avoidance

response was established and they would climb the pole when the buzzer only was sounded.

The testing procedure consisted of placing the rats in the chamber for a 30-second accommodation period, after which the buzzer was sounded for another 30 seconds or until the S would climb the pole. The animal was placed back on the grid, and the US (shock and buzz) was delivered for 30 seconds or until response terminated by the S's climbing the pole. Results showed that control rats typically made the avoidance response within the 30 second intervals before the delivery of the CS and the US. A chlorpromazine dosage of 10.5 mg/kg was found most effective in specifically blocking the conditioned avoidance response to the CS, but the Ss were able to respond to the US. Only at a dosage of 40 mg/kg did the drug block the US in a few animals.

Other research has contributed to the pharmacological profile of chlorpromazine. Verhave, et al., (15) used male rats in research with an apparatus that consisted of a rectangular box with an attached movable brass wheel. The grid floor and three metal walls could be charged electrically (US), and the wheel was the escape area. A muffled buzzer (CS) was presented seven seconds prior to shock and continued for five seconds unless response terminated before that time. Intertrial intervals were varied around a mean of 60 seconds, and Ss were run for 160 or 320 trials per session. Results obtained from Ss which received chlorpromazine doses of 1.6 and 2.5 mg/kg illustrated that the loss of avoidance responses was a function of dosage. Again, dosages of chlorpromazine which abolished most or all avoidance responses were noted to have a relatively minor effect on escape behavior.

Similar selective avoidance results were obtained by Miller, et al., (9) with male rats in a two-compartment conditioning apparatus. During conditioning trials a buzzer was sounded for five seconds or until the

S jumped across a two-inch barrier which separated the two compartments of the apparatus. When the rat failed to avoid within the five-second period, a shock was presented to the grid floor, and the buzzer and shock were terminated when the S made the barrier jumping response. Ss were given 15 preconditioning trials for 15 consecutive days prior to administration of the tranquilizing drug variables. During the chlorpromazine trials Ss were given 10 extinction trials in which the animals did not receive shock if they failed to avoid during the five-second CS interval. Results indicated that chlorpromazine dosages of 0.3, 0.6, and 1.2 mg/kg had respective dosage-related effects on the decrement in avoidance responding.

Results reported on the effects of reserpine on avoidance and escape behavior have generally been similar to those findings reviewed for chlorpromazine. Cook and Weidley (5) used male albino rats in a pole-climbing technique to demonstrate that reserpine specifically blocked the avoidance response to the CS (buzzer) while the animals remained capable of escaping from the US (shock). This same dichotomy of avoidance and escape response selectivity was also observed by Verhave, et al., (15) in a study utilizing a barrier jumping procedure. Weiskrantz and Wilson (16) reported that reserpine severely depressed "avoidance" behavior in their study with Rhesus monkeys. Three judges evaluated S responses to a CS (white noise to which the animals had been preconditioned) which occurred prior to a noxious US (shock). While the monkeys could not respond in such a way as to avoid experiencing the US, the judges evaluated their behavior as any recognizable change in ongoing behavior. All Ss received 10 trials on each of two days, and three days after the second conditioning day the animals were tested (without further injections) for retention of the conditioning response. Ten retention trials were given each day until the Ss met a criterion number of avoidance responses. Monkeys who received

reserpine (.75 mg/kg) showed only slight deviation from "no response" to the noise during conditioning trials but they responded to the shock. Also, tranquilized animals required significantly more training to reach the retention criterion than the control Ss required. Smith, et al., (14) and Pfeiffer, et al., (10) in studies involving shuttlebox techniques also found reserpine functions as an inhibitor of the conditioned avoidance response in monkeys.

Cook and Weidley (5) found that rats receiving meprobamate responded in a qualitatively different way than Ss who had received chlorpromazine or reserpine. Utilizing the same pole-climbing apparatus, they found rats which received meprobamate did not respond selectively to the CS and US, but both avoidance and escape behavior were blocked in many animals. However, the agent blocked these responses only in neurotoxic dose levels (ataxia and semiprostration) when the animals could not make the pole-climbing response because of incapacitation of motor function. Verhave, et al., (15) reported a high dosage (500 mg/kg) of meprobamate caused no clear separation of escape and avoidance loss in male albino rats tested in a wheel-turning apparatus, and animal activity was at a low level during the trials.

Verhave (15), in a review of his own and other studies, has noted that the main point of the studies involving chlorpromazine, reserpine, and other tranquilizers in avoidance learning situations was that the Ss were unable to avoid at dosages where they could make the escape response upon presentation of the US. Verhave concluded that the selective effect on avoidance and escape responses may have considerable generality among the tranquilizers and be independent of the particular response types and apparatus utilized. Meprobamate remains the exception to this generalization, for no clear separation of avoidance and escape loss has been demonstrated for this compound.

Much of the research presently reviewed has been concerned mainly with the initial effect of the tranquilizing agents on avoidance

learning--both acquisition and extinction--and few of the studies have been concerned with the effect these compounds might have on retention or relearning trials given a day or more later when the effects of the drug have diminished or disappeared. Also, the major assumption upon which these experiments have been based was that conditioned fear or anxiety was present and for untranquilized Ss served to mediate in some way learning of the avoidance response. It was assumed that the tranquilizing agents reduced the incidence of fear or anxiety in experimental animals and thus made them less able to learn avoidance behavior. However, these assumptions were subject to criticism, for the presence of fear or its role in mediating behavior had not been clearly demonstrated.

Findings from two recent non-drug studies relate to these considerations. Kamin (8) has studied the retention of an incompletely learned avoidance response. He assumed that if avoidance learning was interrupted before it was completely mastered, only partial retention would occur and a retention curve could be plotted. Kamin used hooded rats in a shuttlebox apparatus. He ran Ss for 25 avoidance learning trials and then gave the animals 25 additional retention trials following delays of 0, 1/2, 1, 6, and 24 hours and 19 days. From his results he plotted a V-shaped retention curve which indicated that retention decreased from 0 to 1 hour and then increased from 1 hour to 24 hours (the "Kamin Effect"). Kamin interpreted the declining section of the curve as a function of "forgetting" and the inclining section of the curve as a function of incubation of the avoidance response. Thus he offered two independent processes to explain the initial decrease and later increase of retention as a function of time interval between avoidance trial sessions. Thus, Kamin's study was a beginning in the attempt to learn about the retention of the avoidance learning response.

Denny's (7) reinterpretation of the Kamin retention curve was relevant to the question of the presence of fear or anxiety in the avoidance learning situation. Denny hypothesized that anxiety initially increased in the interval following the completion of the first 25 avoidance learning trials to a degree that the animal "froze" and was not able to make the avoidance response in the retention series of trials. The freezing was the result of the incubation of anxiety which reached its peak at an interval of approximately one hour and after that decreased so that the retention curve inclined to a point at 24 hours that was not significantly different from that of 0 hours. It was hypothesized that if anxiety could be prevented from incubating the Kamin retention curve could be eliminated.

Denny, with some variations, repeated the Kamin experiment by utilizing delays of 0, 1, and 24 hours. Two different procedures were employed to inhibit the incubation of anxiety during the one-hour delay interval. One group of Ss was under a reduced food plan for two weeks and subject to 24-hour food deprivation prior to the trials. These rats were permitted to eat alone in their home cages during the one-hour delay. Another group of Ss remained in the shuttlebox during the interval with the presence of the buzzer or shock (desensitization). Denny also hypothesized that if animals were given the same amount of shock received in the initial learning series in trials the following day and in another situation, then the incubation of anxiety following such second-day trials would produce the Kamin Effect in further training trials given one hour later. Data from the procedures supported the incubation of anxiety hypothesis.

Thus, Kamin's study has introduced the problem of retention (or relearning) of an avoidance learning response, and Denny's research has given support to the assumption of the presence of anxiety in the avoidance learning situation. The role of anxiety, however, remains

obscure. Denny's results indicated that the incubation of anxiety following an initial 25 trials continued to an "excessive" point so that the animal froze and was unable to make the avoidance learning response. The present review of other research with tranquilizing agents has indicated that the removing or blocking of anxiety by the drugs even more completely reduced the avoidance learning response. An answer to this paradoxical problem might be that a certain intermediate level of anxiety is essential for the S to learn avoidance behavior, i. e., tranquilization reduces the level of anxiety too much for learning, and the incubation of anxiety following an initial learning series of trials increases the level of anxiety too much for avoidance learning. While the function of anxiety in avoidance learning is not clear, its demonstrated presence in such situations makes the use of tranquilizing drug variables relevant in avoidance learning research.

One purpose of the present study was to contribute behavioral, pharmacological information about Stelazine,¹ a Phenothiazine derivative, so that this relatively unknown tranquilizing agent may be related to other compounds to which it is similar in chemical structure (e. g., chlorpromazine, etc.) and to tranquilizing drugs in general. Another purpose was to learn some of the effects of a tranquilizing drug on the retention (relearning) of avoidance learning behavior.

¹The only pharmacological information relative to the effects of stelazine on avoidance behavior found by this experimenter was an unpublished laboratory report from Smith, Kline, and French, the manufacturers of the compound. The following comparative dosages necessary to produce 80% blockage of a conditioned avoidance response were: stelazine--7.4 mg/kg, chlorpromazine--18.0 mg/kg, and prochlorpromazine--9.8 mg/kg. The dosages necessary to produce 20% blockage of an unconditioned response were as follows: stelazine--17.2 mg/kg, chlorpromazine--30.0 mg/kg, and prochlorpromazine--0.8 mg/kg. These comparisons of stelazine with the two compounds most similar to it in chemical structure, chlorpromazine and prochlorpromazine, revealed that stelazine is considerably more specific in its blocking action than any of the other compounds.

Answers to the following specific questions were sought during the present research:

- (1) Is there an effect of stelazine on initial avoidance learning?
- (2) Is there an effect of stelazine on relearning when the original avoidance learning occurred without tranquilization?
- (3) Is there an effect on untranquilized relearning when the original training occurred under stelazine?

II. METHOD

Subjects

Fifty experimentally-naive hooded rats from the colony of the Department of Psychology of the Michigan State University and ranging in age from 158 to 224 days at the beginning of the study were the Ss. Prior to and during the research the 37 male and 13 female animals were housed in cages containing from three to five Ss of the same sex and were maintained on ad lib food and water schedules. The rats were divided randomly into five groups of ten animals each except that approximately the same ratio of males and females was maintained in each group.

Apparatus

All animals were tested in a modified Mower-Miller shuttle box which was painted flat black and which had a glass front for observation by the experimenter. The shuttle box was 36 inches long, 14 inches high, and 4 inches wide with a hinged ceiling and a grid floor. The gridway was made of copper rods placed approximately 1/4 inch apart, and each half of the gridway could be electrically charged independently of the other half. (The gridway was continuous for the length of the shuttle box with no barrier in the middle.) A continuous flow of 1.7 milliamps of electricity was supplied directly to the grid rods via a C. J. Applegate stimulator, and the Ss completed the circuit of current (and thus caused the shock) when they made contact with any two adjacent grid rods. A seventy decibel electric buzzer (activated by six dry cells) served as a conditioned response and was attached to the outside

of one end of the shuttle box. Three separate toggle switches were located on a control panel and permitted independent control of each half of the gridway and the buzzer. The control panel was placed near the shuttle box and alongside a stopwatch so that the experimenter was able to observe the animal, operate the switches, and record the data with a minimum of movement.

A waiting cage, approximately 16 inches long, 6 inches high, and 6 inches wide was used to house the Ss in the interval between real or sham injections and the beginning of the learning sessions. The interior of the cage was semi-dark because light could enter only from the wirecloth front, and the cage was placed in a quiet experimental room.

Procedure

The experiment was divided into two sessions so that all Ss from every group were given two identical avoidance learning sessions--an initial incomplete learning series (Session I) including 25 avoidance learning trials followed 48 hours later by a second relearning phase (Session II) including 25 additional trials. The Ss were kept in their home cages under normal conditions during the inter-session period.

During any given session the S was placed in the shuttle box for a one minute orientation period before the trials began. The buzzer (CS) was sounded for five seconds before the shock (US) began and was response terminated if the animal crossed the midline of the gridway during that time (avoidance). If the animal failed to avoid, the CS and US occurred together and were both response terminated when the animal crossed the midline (escape) or after 35 seconds had elapsed. The inter-trial interval (time between successive CSs) was one minute. For those times when S avoided on the initial (one or more) trials of a series, these trials were not counted as part of the 25 trials so that

the first trial of the 25 was one where the rat received the US after having failed to respond to the CS.

Ss from the various groups received different combinations of the following four types of treatments prior to their Session I and Session II trials: Sham Injection--the rat was taken from his home cage into an experimental room, held upside-down on the lap of the experimenter, rubbed on the ventral midsection with alcohol, punctured subcutaneously with a hypodermic needle, rubbed again with alcohol, and then placed in a waiting cage for 15 minutes prior to the beginning of the session. No Sham Injection--the animal was taken directly from his home cage, and was immediately ready for the experimental session. Dosage 0.25 mg/kg--the S was moved from his living quarters into the experimental room, injected subcutaneously in the ventral midsection with a solution including 3.75 mg stelazine per 50 cc. physiological saline so that each animal received a stelazine dosage of 0.25 mg/kg of body weight, and placed in the waiting cage for 15 minutes prior to the beginning of the block of trials. Dosage 0.15 mg/kg--these Ss received treatment identical to that described for Dosage 0.25 mg/kg except that the stelazine dosage was 0.15 mg/kg of animal weight. All the rats used in the experiment were weighed immediately following their initial removal from the home cage prior to the Session I block of learning trials.

Pre-session treatment combinations for the five groups of Ss were assigned as follows: Group A (control) animals received a Sham Injection before Session I and another Sham Injection prior to Session II; Group B rats were given No Sham Injection before Session I and Dosage 0.25 mg/kg before Session II; Group C Ss received No Sham Injection and Dosage 0.15 mg/kg prior to Sessions I and II respectively; Group D animals were given Dosage 0.25 mg/kg before Session I and Sham Injection prior to Session II; and Group E rats received Dosage 0.15 mg/kg and Sham Injection before Sessions I and II respectively.

Summary of Pre-Session Treatments

<u>Group</u>	<u>Session I</u>	<u>Session II</u>
A (Control)	Sham Injection	Sham Injection
B	No Sham Injection	Dosage 0.25 mg/kg
C	No Sham Injection	Dosage 0.15 mg/kg
D	Dosage 0.25 mg/kg	Sham Injection
E	Dosage 0.15 mg/kg	Sham Injection

III. RESULTS

A Studentized Distribution was used to compare separately the mean total avoidance responses of the groups in Session I and Session II, and Group B I (No Sham) and Group C I (No Sham) mean responses were pooled together as one mean because they were obtained from Ss which had received identical Session I treatment. The analysis is summarized in Table 1 and indicates the following significant differences at the .05 level (See Table 1, page 15): (1) Rats which received No Sham Injections in Groups B I and C I made more avoidance responses than Ss in Group D I which were given the larger dosage (0.25 mg/kg) of Stelazine; (2) More avoidance responses were completed by control Ss (Group A I) who received sham injections than were made by animals in Group D I which had been administered 0.25 mg/kg of drug; and (3) During Session II more avoidance responses were recorded for Group A II (Control) rats, which received sham injections, than were made by Group D II Ss which were given sham injections after having received a 0.25 mg/kg dosage during the prior Session I trials. A comparison between the mean responses of Group A I (Control--Sham Injection) and the mean avoidances of Ss in the pooled No Sham B I and C I Groups revealed that these two types of pre-session treatments were not significantly different. Finally, comparisons of the Group E I mean (Ss received the lighter dosage of 0.15 mg/kg) were not significantly different from the means of the Groups (A I and B I plus C I) whose Ss had received no drug or the mean of Group D I whose rats received the high dosage (0.25 mg/kg). These t values thus indicated that the Group E I mean holds an intermediate position somewhere between the No Drug Group (A I and B I plus C I) means which are significantly different from the larger dosage (0.25 mg/kg) mean of Group D I.

Table 1--Summary of Studentized t Ratios of Group-Session Means
Based on the Number of Avoidance Responses

Group-Session	<u>N</u>	<u>M</u>	<u>t</u>	<u>P</u>
A I	10	9.5	0.092	---
B I + C I	20	9.3		
B I + C I	20	9.3	3.09	.05
D I	10	2.6		
B I + C I	20	9.3	1.66	---
E I	10	5.7		
E I	10	5.7	1.238	---
D I	10	2.6		
A I	10	9.5	2.755	.05
D I	10	2.6		
A I	10	9.5	1.517	---
E I	10	5.7		
C II	10	11.3	0.493	---
B II	10	9.7		
A II	10	13.9	1.211	---
B II + C II	20	10.5		
E II	10	9.7	1.573	---
D II	10	4.6		
A II	10	13.9	2.404	---
D II + E II	20	7.15		
A II	10	13.9	2.87	.05
D II	10	4.6		
A II	10	13.9	1.296	---
E II	10	9.7		

A plot of the culminative mean avoidance responses for blocks of five trials from all groups in Session I and Session II is presented in Figure 1, page 17. The Session I section of Figure 1 indicates that the means of Groups A I, B I and C I, whose Ss received Control and No Drug treatments, had progressively higher averages than the intermediate means of Group E (0.15 mg/kg) and the lower means of Group D I (0.25 mg/kg). Control Group A II (Sham) means in the Session II plot were consistently higher than the averages of any of the experimental groups, and Group C II (0.15 mg/kg) means were greater than those of Group B II (0.25 mg/kg) whose Ss received a larger drug dosage prior to Session II trials. Finally, Group E II and Group D II Ss, which were given Session II sham injection treatment similar to that given to A II control animals, produced response averages which were correspondingly lower, in terms of the Session I dosages received by these Ss, than the Group A II means.

Shown in Table 2 below is a summary of t values based on the mean difference between the number of Session I and Session II avoidance responses for each S.

Table 2--Summary of t Values Based on the Mean Difference Between the Number of Avoidance Responses in Session I and Session II for Each Subject

Group	<u>N</u>	<u>D</u>	<u>t</u>	<u>P</u>
A	10	4.4	2.14	.05
B	10	0.0	0.0	---
C	10	2.4	1.78	---
D	10	2.0	1.52	---
E	10	4.0	2.21	.05

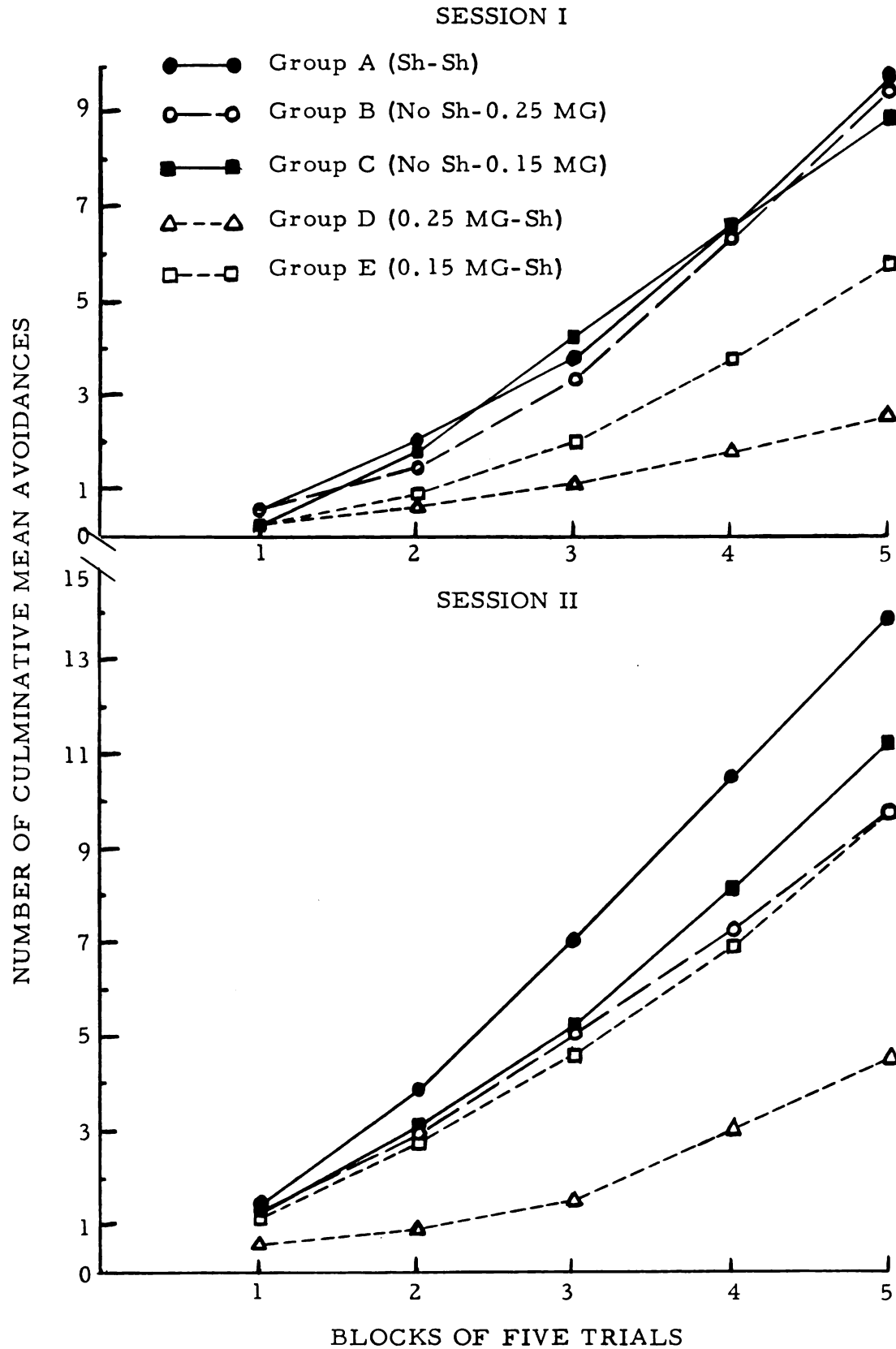


Figure 1. Distribution of Culminative Mean Avoidance Responses from All Groups in Session I and Session II.

Significant differences at the .05 level were obtained between the Session I and Session II means for control Group A (Sham-Sham) and for Group E whose Ss received the 0.15 mg/kg and Sham treatments respectively prior to each session. The distribution of the improvement of the mean total avoidance responses of Session II over Session I for each group is graphed in Figure 2, page 19. Group B (No sham--0.25 mg/kg) Ss showed no improvement, and Group C (No Sham--0.15 mg/kg) Ss with the lighter dosage gave moderate improvement. Finally, rats in Group D improved only moderately after having the large dosage and Sham treatments prior to Session I and Session II respectively.

The mean reaction latencies (Appendix B) of the animals were analyzed in the same way as the avoidance responses, and significant differences were obtained for most of the comparisons which were found to be significantly different in the avoidance response analysis. Product-moment correlations of the total avoidance responses with the total reaction times for each of the fifty Ss yielded coefficients of .56 for Session I data and .67 for Session II results, and both of these coefficients, significant at the .01 level, indicated a negative correlation between number of avoidances and latency time. Thus, the two variables appeared to measure essentially the same phenomenon.

Occasionally an animal which failed to make the avoidance response also failed to escape when the shock was presented. However, no group included significantly more of these Ss than any other group, and the number of rats in each group who did not make 25 escapes during both sessions were as follows: Group A--3, Group B--2, Group C--2, Group D--4, and Group E--4.

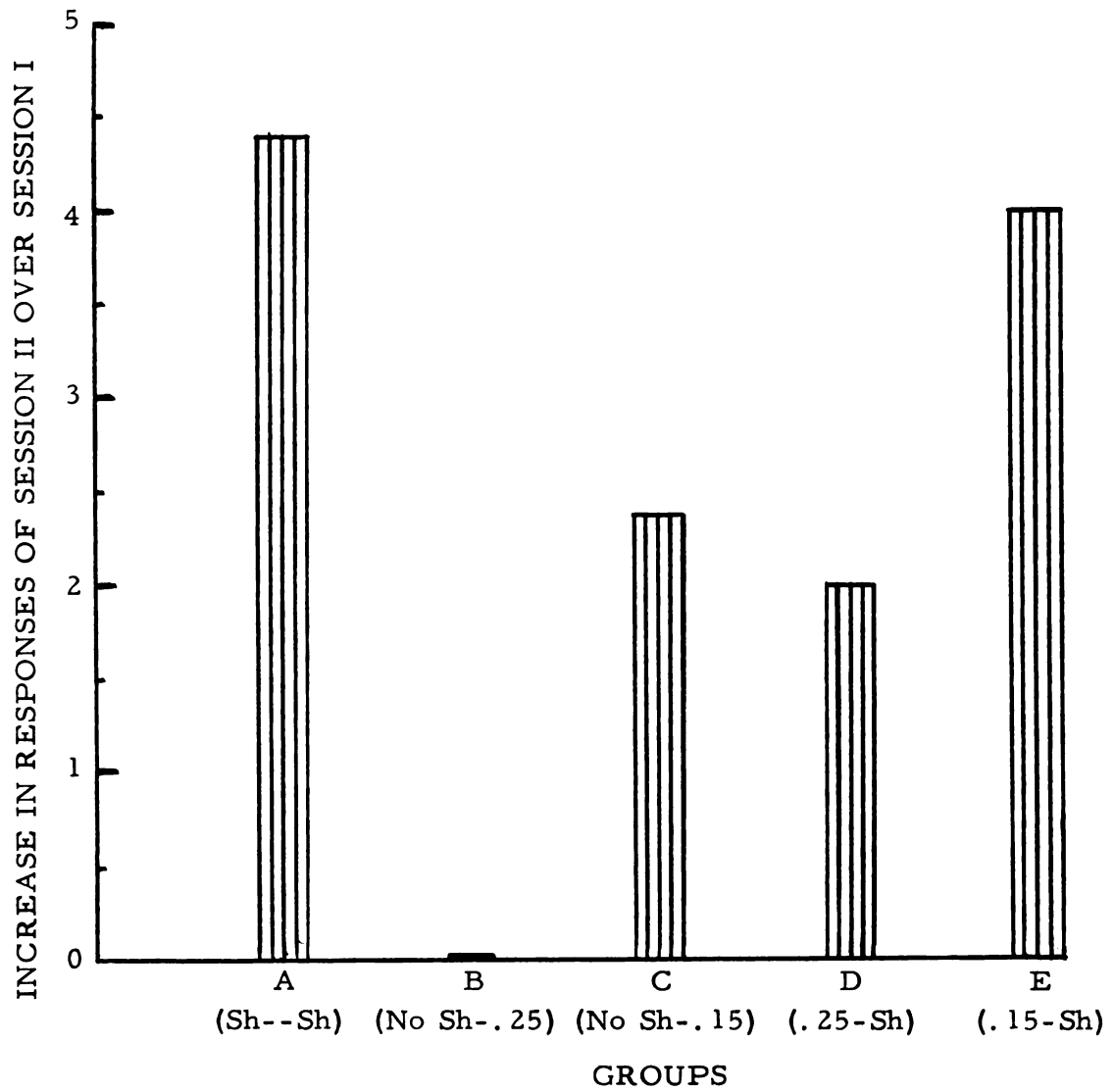


Figure 2. Distribution of the Improvement of the Mean Total Avoidance Responses of Session II over Session I for each Group.

IV. DISCUSSION

Results of the present investigation indicated that the effects of stelazine in the avoidance learning situation are similar to those of the other Phenothiazine derivative--chlorpromazine and the Rauwolfia Alkaloid--reserpine. Consequently it was also found that the effects of stelazine differ qualitatively from those of the Substituted Propanediol--meprobamate as was reported by Cook and Weidley (5) and Verhave, et al., (15).

The reduced number of conditioned avoidance responses of the drugged Ss in Session I appear to be a function of dosage as suggested by Verhave, et al., (15) and Miller, et al., (9), and the moderate effect of the smaller dosage indicates an unusual potency of stelazine as compared with other tranquilizing agents. A search of the literature revealed no other studies where a tranquilizing compound dosage of less than 0.25 mg/kg yielded observable effects. The drug's effect was a specific blocking of the avoidance response to the buzzer (CS) while the Ss generally were able to make the escape response from the shock (US); and this selective reaction was accompanied by longer response latencies. This type of behavior has been reported by others (5, 15, 16) for both chlorpromazine and reserpine. This specific blocking of avoidance behavior in drugged Ss suggests that the reduced number of avoidance responses (and longer reaction times) may be a function of some type of reduction (or blockage) of anxiety or fear, and this reduced anxiety may interfere with the "excitation" level required for the organism to make the higher order (or more central) type of learning response. The rat remains able to perform lower level (or less central) behavior such as "alerting" to the CS and running to

escape when the US is presented, although it may take him longer, in the case of larger dosages, to "decide" to make the escape. The delayed reaction times particularly for higher dosage Ss suggest that these animals may have been close to a point of tranquilization which would have prevented both the higher and lower level types of response, and further research may show that higher dosages of stelazine will eliminate the selective responses noted in the present and other research. The probability that the selective avoidance response is a function of motor incapacitation or sensory diminution, as suggested by Brady (3), does not appear tenable because the rapid running escapes of Ss from shock, however delayed, indicated serviceable motor coordination (9), and the "alerting" of the Ss to the CS and the escapes from the US showed at least a degree of aural and "pain" sensitivity. The longer latencies did not appear to result from the Ss' motorial inability to execute the responses, but rather they may have been a function of a higher level control which determined how and when to respond.

Results from the present research also indicated that stelazine had an inhibiting effect as a function of dosage on the improvement of learning by those Ss who made the original learning trials under non-drugged conditions, but these rats were able to maintain the level of avoidance learning achieved in the initial session. Again, the Ss were inhibited for new learning, and the maintenance of the previous level of learning might be explained by the hypothesis that once a response has been learned (acquisition) a lower level type of control is required for its maintenance. An interesting finding of this study was that Ss which received the larger dosage during the initial trials made only moderate improvement during the relearning series (given without the drug), and these animals were not able to attain a level of avoidance responding comparable to that level achieved by non-drugged Ss during original

learning trials. In other words, the 0.25 mg/kg dosage not only inhibited the S's ability to make the avoidance response initially, but there was some kind of carryover effect which functioned to inhibit the rat's ability to achieve a level of performance in relearning trials which is typical for non-drugged animals in initial training sessions. The experience of not avoiding during the initial trials may have been impressed (conditioned) at a lower level of control, and this behavior had to be extinguished before the S could learn to avoid. Thus a greater number of trials may have been required to extinguish the non-avoiding behavior (which was established at a lower level of control) when the animal later was under a non-drugged, higher level type of control.

V. SUMMARY

The present research was designed to study the effects of the tranquilizing drug, stelazine, on avoidance learning and relearning. Thirty-seven male and 13 female hooded rats were given 25 avoidance learning trials in a modified Mower-Miller shuttle box, and these initial trials were followed 48 hours later by 25 additional relearning trials. The results indicated that 0.25 mg/kg of stelazine significantly reduced initial avoidance learning, correspondingly increased response latencies, and did not affect Ss' ability to make the escape response, and this same dosage when given for the initial trials functioned to reduce relearning and increase latencies in later trials when the animals were not drugged. Also, stelazine interfered with the improvement of learning (and the reduction of latencies) of the second series of trials over the initial trials, but the drug did not reduce the level of learning below that which had been attained in initial training. The findings were tentatively interpreted in terms of stelazine's reduction of an intermediate level of anxiety which may be necessary for rats to learn avoidance.

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APPENDIX A

SUMMARY OF AVOIDANCE RESPONSE DATA

Rat Number	Total Avoidance Responses														
	Group A			Group B			Group C			Group D			Group E		
	Ses I	Ses II	Sh	Ses I	Ses II	Sh	Ses I	Ses II	Sh	Ses I	Ses II	Sh	Ses I	Ses II	Sh
	Sh ^a	.25 ^b		No	No		No	No		No	No		No	No	
1	7	11		4	6		18	21		1	1		0	1	
2	3	14		14	16		0	0		8	4		1	7	
3	11	10		14	16		4	14		8	11		2	2	
4	19	19		12	1		7	3		2	9		7	9	
5	20	14		18	11		5	3		0	1		15	20	
6	15	17		17	16		7	7		0	0		3	0	
7	12	22		4	0		9	13		0	4		11	11	
8	0	10		2	3		6	9		5	6		0	2	
9	6	20		1	5		20	22		0	10		8	24	
10	2	2		11	23		13	21		2	0		10	21	
<u>M</u>	9.5	13.9		9.7	9.7		8.9	11.3		2.6	4.6		5.7	9.7	
<u>SD</u>	7.04	5.95		6.37	7.8		6.29	8.18		3.22	4.22		5.24	9.04	

^a Sham operation given 15 minutes before session.

^b Dosage of .25 mg/kg given 15 minutes before session.

^cDosage of .15 mg/kg given 15 minutes before session.

Table A-2--Summary of Avoidance Response Data

Subjects		1 2 3 4 5 6 7 8 9 10										Mean	1 2 3 4 5 6 7 8 9 10										Mean
Blocks of 5 Trials		Session I											Session II										
Group A (Sham - Sham)	1	0	1	0	1	1	1	0	0	1	0	0.5	0	0	2	4	1	0	3	0	3	1	1.4
	2	2	1	2	4	4	1	1	0	0	0	1.5	1	1	3	3	2	4	5	1	4	0	2.4
	3	1	1	1	5	5	3	2	0	0	0	1.8	3	3	2	4	4	5	5	3	3	0	3.2
	4	2	0	4	5	5	5	4	0	1	1	2.7	4	5	2	3	4	4	4	4	5	0	3.5
	5	2	0	4	4	5	5	5	0	4	1	3.0	3	5	1	5	3	4	5	2	5	1	3.4
Group B (No Sh-. 25)	1	0	0	1	0	2	1	0	0	1	0	0.5	1	2	2	0	0	3	0	0	0	4	1.2
	2	0	2	3	0	3	2	0	0	0	0	1.0	2	5	2	0	0	2	0	1	0	5	1.7
	3	0	3	3	3	4	5	0	0	0	1	1.9	1	2	4	1	2	5	0	2	0	5	2.2
	4	2	5	3	5	3	5	2	0	0	5	3.0	0	4	4	0	4	3	0	0	2	5	2.2
	5	2	4	4	4	5	5	2	2	0	5	3.3	2	3	4	0	5	3	0	0	3	4	2.4
Group C (No Sh-. 15)	1	1	0	0	0	0	1	0	0	0	0	0.2	3	0	1	1	0	0	1	0	4	3	1.3
	2	3	0	0	3	1	2	1	1	5	1	1.7	4	0	3	0	0	0	2	0	4	4	1.7
	3	4	0	0	3	2	0	4	1	5	4	2.3	4	0	4	0	0	1	3	0	5	4	2.1
	4	5	0	3	0	1	0	1	3	5	4	2.2	5	0	2	1	2	3	2	5	5	5	3.0
	5	5	0	1	1	1	4	3	1	5	4	2.5	5	0	4	1	1	3	5	4	4	5	3.2
Group D (. 25-Sh)	1	0	0	0	0	0	0	0	1	0	0	0.1	0	0	1	1	0	0	0	2	1	0	0.5
	2	0	3	0	0	0	0	0	2	0	1	0.6	1	0	2	0	0	0	0	0	1	0	0.4
	3	0	0	1	2	0	0	0	0	0	1	0.4	0	0	1	0	1	0	0	2	2	0	0.6
	4	0	2	4	0	0	0	0	1	0	0	0.7	0	3	4	3	0	0	1	1	3	0	1.5
	5	1	3	3	0	0	0	0	1	0	0	0.8	0	1	3	5	0	0	3	1	3	0	1.6
Group E (. 15-Sh)	1	0	0	0	0	1	0	0	0	1	0	0.2	0	0	1	0	3	0	0	0	4	3	1.1
	2	0	0	0	1	1	0	0	0	1	3	0.6	0	0	0	2	3	0	2	0	5	4	1.6
	3	0	0	1	1	3	2	3	0	2	0	1.2	0	0	0	2	5	0	2	1	5	4	1.9
	4	0	1	0	1	5	1	4	0	2	3	1.7	0	2	1	1	5	0	4	0	5	5	2.3
	5	0	0	1	4	5	0	4	0	2	4	2.0	1	5	0	4	4	0	3	1	5	5	2.8

APPENDIX B

SUMMARY OF LATENCY DATA

Table B-3--Summary of t Ratios of Group-Session Means Based on the Response Latencies of All Subjects

Group-Session	<u>N</u>	<u>M</u> ^a	<u>t</u>	<u>P</u>
A I	10	6.16	0.399	---
B I + C I	20	5.67		
B I + C I	20	5.67	2.668	.025
D I	10	13.88		
B I + C I	20	5.67	1.491	---
E I	10	9.05		
E I	10	9.05	1.294	---
D I	10	13.88		
A I	10	6.16	2.409	.025
D I	10	13.88		
A I	10	6.16	1.184	---
E I	10	9.05		
C II	10	5.41	0.177	---
B II	10	5.15		
A II	10	4.53	0.720	---
B II + C II	20	5.28		
E II	10	10.37	0.476	---
D II	10	9.17		
A II	10	4.53	3.589	.005
D II + E II	20	9.77		
A II	10	4.53	3.083	.005
D II	10	9.17		
A II	10	4.53	2.566	.025
E II	10	10.37		

^aTime, in seconds, from onset of CS to offset of CS or offset of CS and US combined.

Table B-4--Summary of $\bar{t}$ Values Based on the Average Difference
Between the $\bar{M}$ Mean Response Latencies in Session I and
Session II for Each Subject

Group	$\bar{N}$	$\bar{D}$	$\bar{t}$	$\bar{P}$
A	10	1.63	2.278	.025
B	10	0.09	0.13	----
C	10	0.68	0.686	----
D	10	4.71	2.015	.05
E	10	-1.32	-0.215	----

Table B-5--Summary of Mean Latencies for Subjects of All Groups for Session I and Session II

Mean Latencies														
Group A			Group B			Group C			Group D			Group E		
Rat Number	Ses I	Ses II	Ses I	Ses II	Ses I	Ses II	Ses I	Ses II	Ses I	Ses II	Ses I	Ses II	Ses I	Ses II
	Sham	Sham	No Sh	.25	No Sh	.15	No Sh	.25	No Sh	.15	No Sh	.25	No Sh	.15
1	7.0	4.0	4.0	6.0	3.4	3.7	3.4	6.5	8.7	14.0	12.0			
2	2.5	3.0	2.0	3.7	8.5	13.9	8.5	6.0	7.0	23.5	18.0			
3	3.0	3.0	5.0	5.0	9.0	4.0	9.0	10.0	8.0	6.0	18.0			
4	5.0	5.2	4.5	3.0	9.0	6.0	9.0	7.0	5.3	4.0	3.0			
5	4.0	4.0	4.0	4.0	5.0	7.0	5.0	25.5	15.4	6.0	17.0			
6	4.6	3.0	4.5	6.0	7.0	5.0	7.0	30.0	12.5	5.0	8.0			
7	4.0	4.3	3.0	3.5	4.0	5.0	4.0	6.5	6.3	18.0	17.0			
8	10.0	6.0	12.0	13.5	5.5	5.0	5.5	5.5	5.0	4.5	1.5			
9	8.5	2.3	5.0	5.5	2.5	2.0	2.5	24.0	7.0	4.5	3.0			
10	13.0	10.5	8.4	2.0	7.0	2.5	7.0	18.0	16.5	5.0	6.2			
M	6.16	4.53	5.24	5.22	6.09	5.41	6.09	13.88	9.17	9.05	10.37			
SD	3.41	2.328	2.896	3.24	2.366	3.34	2.366	9.55	4.15	6.93	6.81			

APPENDIX C

COMPARISON OF AVOIDANCE AND LATENCY DATA

Table C-6--Comparison of Mean Avoidances with Mean Latencies for Ss in All Groups for Session I
and Session II

Group-Session	A I	A II	B I	B II	C I	C II	D I	D II	E I	E II
Mean Avoidances	9.5	13.9	9.7	9.7	8.9	11.3	2.6	4.6	5.7	9.7
Mean Latencies	6.2	4.5	5.2	5.2	6.1	5.4	13.9	9.2	9.1	10.4

FILE ONLY

