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A Parametric Analysis of Memory Retrieval In A Drug Dependent Learning Paradigm

James Kyle Timmons
Kansas State College of Pittsburg

A PARAMETRIC ANALYSIS OF MEMORY RETRIEVAL IN A DRUG DEPENDENT LEARNING PARADIGM

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By

James Kyle Timmons

KANSAS STATE COLLEGE OF PITTSBURG

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TABLE OF CONTENTS

CHAPTER		PAGE
I.	INTRODUCTION	1
	History of State Dependent Learning Research	1
	Disruption of dissociated learning	11
	Alcohol and state dependent learning	12
	Problem	12
	Hypothesis	13
	Significance of the study	13
II.	METHOD	14
	Subjects	14
	Apparatus	14
	Drugs	15
	Procedure	15
III.	RESULTS	18
IV.	DISCUSSION	27
APPENDIX A.	FIGURES	28
APPENDIX B.	TABLES	36
REFERENCES		48

Abstract

State-Dependent learning (SDL) is the failure of learning to transfer from one drug state to another. State dependent learning was demonstrated and disrupted in an escape learning task. Male hooded rats were trained to escape shock in a modified T-maze. The rats were trained in either the drug (ethyl alcohol) state or the non-drug (water) state. The Transfer (T) group of rats were subjected to a 1 kHz tone during training and testing. The SDL groups were not. The results indicated that disruption of state dependent learning occurred in the T groups. That is, learning transferred across drug states. This was not the case with the SDL groups. This transfer of learning was attributed to the role of the tone as an emotional memory prompter.

LIST OF TABLES

TABLE		PAGE
I.	Training, Correct Turns, All Groups.	36
II.	Training, Correct Turns, Experimental Groups	37
III.	Training, Correct Turns, Control Groups.	38
IV.	Mean Median Latencies, Training, All Groups.	39
V.	Mean Median Latencies, Training, Experimental Groups . .	40
VI.	Mean Median Latencies, Training, Control Groups.	41
VII.	Testing, Correct Turns, All Groups	42
VIII.	Testing Correct Turns, Experimental Groups	43
IX.	Testing Correct Turns, Control Groups.	44
X.	Mean Median Latencies, Testing, All Groups	45
XI.	Mean Median Latencies, Testing, Experimental Groups. . .	46
XII.	Mean Median Latencies, Testing, Control Groups	47

LIST OF FIGURES

FIGURE PAGE

1. Number of correct turns for the first and last 4 days of training for the experimental groups. 28

2. Number of correct turns for the first and last 4 days of training for the control groups. 29

3. Number of correct turns for the five days of testing for the experimental groups. 30

4. Number of correct turns for the five days of testing for the control groups. 31

5. Means of the median latencies for the first and last 4 days of training for the experimental groups. 32

6. Means of the median latencies for the first and last 4 days of training for the control groups. 33

7. Means of the median latencies for the five days of testing for the experimental groups. 34

8. Means of the median latencies for the five days of testing for the control groups 35

CHAPTER I

INTRODUCTION

History of State Dependent Learning Research

State dependent, or dissociated learning is learning which occurs in a given drug state and can be recalled only in that drug state. Scientists have only recently began to study state dependent learning, however, the concept is not new. References to state-boundness occur in literature as early as 1538 (Fischer and Landon, 1972).

Scientific study of state-dependent learning in this century began in the 1930's. State dependent learning research began as a facet of neural learning theory research. Edward Girden (1940, 1942 a,b,c, 1947) and Girden and Culler (1937) began extensive research on conditioned responses under curare and derivatives of curare. Harlow and Stagner (1933) studied the effects of muscle paralysis upon learning by conditioning cats and dogs while under curare. They concluded "that preservation of stimuli alone will not cause learning if no reaction is made" (Harlow and Stagner, 1933; p. 293).

Harlow and Stagner's findings disagreed with the findings of Crisler (1930) who studied the salivary conditioned reflex in dogs under the influence of morphine and atropine. Crisler concluded that a conditioned reflex was established in spite of the fact that the drug-state of the dogs prevented them from producing an effector response.

Light and Gantt (1936) reported that the response to a stimulus does not have to be present during the training period in order for the response to be learned. It should be noted that Light and Gantt's research did not involve the use of drugs to block the conditioned response. Instead, the nerve was crushed, the animal conditioned, and later (when the nerve had regenerated), tested.

Girden and Culler also dispute the theory of Harlow and Stagner. Girden and Culler state the "isolated muscles such as the semi-tendinosus are capable of response (a slight twitch in response to electric shock)" (Girden & Culler, 1937; p. 273). Girden and Culler also state that "such responses (furthermore) are susceptible to conditioning to the sound of a bell" (Girden & Culler, 1937; p. 273). Girden and Culler explain the failure of previous investigators to obtain a conditioned response under curare as a result of the fact that they always tested for the conditioned response after the animal was returned to the non-drug state. Thus, the phenomenon of dissociation itself was possibly responsible for the absence of a conditioned response.

Girden (1940) again challenges the research of Harlow and Stagner on the grounds that curare not only diminishes the intensity of the animal's response, but also produces qualitative changes as well. In his 1940 article, Girden advanced the idea that learning occurred at both the cortical and sub-cortical levels. Girden theorized learning in the normal (non-drug) state was mediated by cortical pathways, and that learning of a conditioned response while under the influence of curare was mediated by sub-cortical pathways.

That is, the curare lowered the level at which the brain functioned. Girden hypothesized that curare produced a "functional decortication." To test this hypothesis, Girden removed "both sylvian areas and the large surrounding ectosylvian gyri" (cortical auditory areas). Girden (1940) found that:

> . . . . when a reaction to the cortical pathway is literally extripated, the block between normal and curare states is disrupted; the CR's (conditioned reflexes) established in either one of the two conditions will now be manifested in the other state. (p. 404)

Girden's research dealt primarily with autonomic aspects of behavior. In another attempt to test his "cortical/sub-cortical" theory of dissociated learning, Girden (1942a) studied the dissociation of pupillary conditioned reflexes. The drugs used to produce dissociation were crude curare and erythroidine (a curare-form drug). In this research, Girden found that conditioned reflexes developed in the drug state were absent when the animal was in the non-drug state, and that the conditioned reflexes reappeared upon reintroduction of the drug state.

An experiment in which blood pressure responses were used as conditioned responses collaborated Girden's earlier findings with respect to dissociation. Again, Girden found that "all elements of the drug state are completely repressed upon recovery from the drug (Girden, 1942b; p. 230). Girden attempted to define his "cortical/sub-cortical" dichotomy more sharply in a 1943 experiment.

He conditioned animals to respond in a "deep state" of drug intoxication and then tested them for retention of the responses in both a "mild" drug state and a drug-free state. Girden again found complete dissociation between the "deep" drug and non-drug states, and he also reported that animals trained in the deep drug state did not produce striated muscle responses in the mild drug state (Girden, 1943).

Girden (1943) also found that if responses mediated by the central nervous system were not made during the training period, they did not occur later. This finding may help resolve the dispute over the necessity of a response to learning. Girden's results bring to mind the possibility that the necessity of a response may depend upon the level of a given response (for example ANS as opposed to CNS). Another major finding of this research was the demonstration by Girden of dissociation between varying dosages of the same drug, as well as between drug and non-drug states. Using curare, Girden (1947) also demonstrated state dependent learning in monkeys. These findings were consistent with the results of his earlier experiments in which dogs were used. Another finding worth noting is that Girden reports learning in the drug state is at least as efficient, or possibly more efficient, than in the non-drug state.

In summary, Girden's main contribution to the field of state dependent learning research was his experimental demonstration of the phenomenon itself; or, as Girden wrote: "The drug state learning is repressed upon recovery from the drug state, and reappears

spontaneously upon reintroduction of the drug state" (Girden, 1947; p. 587).

In 1962, Soloman and Turner attempted to test the ideas of Girden. Contrary to Girden, Soloman and Turner reported that dogs tested in the non-drug state "responded in a way consistent with their discriminative Pavlovian conditioning experience under curare" (Soloman and Turner, 1962; p. 218). These findings cast doubt on the research of Girden. However, the discrepancies between the two findings can be explained.

Girden used crude curare in his experiments. Crude curare is known to act on the central nervous system. Whereas, Soloman and Turner used d-tubocuraine, a curare derivative which does not exhibit its main effects on the central nervous system.

Sachs, Weingarten and Klein (1966) found dissociated learning using chlordiazepoxide (Librium) to produce the drug state. A CAR (conditioned avoidance response) was used. Rats were trained to avoid shock in a hurdle jump task after injections of chlordiazepoxide (drug state) or saline (non-drug state). Sachs, et. al. reported dissociation of learning between drug and non-drug states.

Sachs, et. al. (1966) suggested that the dissociative effect in state dependent learning was due to central nervous system effects. This finding was significant in that it helped to resolve basic questions about the nature of state dependent learning. Sachs, et. al. note the superiority of central nervous system depressants in producing dissociation. This finding helps to reconcile the differences between Girden's findings and the findings

of Soloman and Turner. Sachs, et. al. also theorized that the dissociative effects of drugs are limited to a specific region of the brain, as opposed to the entire central nervous system. Another significant contribution by Sachs, et. al. was the finding that chlordiazepoxide (CDP), or Librium, was very effective in producing dissociation (Sachs, et. al., 1966).

Overton (1964, 1966, 1967, 1968) has been a major contributor to the area of state-dependent learning research in the past decade. Overton (1964) reported nearly complete dissociation of learning in rats trained in a maze to turn in one direction under the influence of Sodium Pentobarbital and in the other direction when in the non-drug state. In the same publication, Overton also reported nearly complete dissociation between states as measured by an absence of savings between groups. This finding is significant because the use of the savings method in measurement is considered a stricter criterion than the previously reported tests. Also in the same paper, Overton reported that rats could be trained concurrently in both drug states as opposed to the previous method of training completely in one state before initiating training in the opposite state. Once again, Overton reported that learning was dissociated. Overton also reported an inverse relationship between the amount of pentobarbital used and the amount of transfer of learning between drug and non-drug states. In other words, the heavier the dosage, the greater the amount of dissociation. These results led Overton to conclude that "it is possible to find two drug states between which any desired amount of transfer of training

will occur" (page 8). In the final experiment reported in his 1964 article, Overton compares the degrees to which various drugs and single and multiple external stimuli acquire control of responses. He reports that pentobarbital and multiple external stimulus changes acquired control over responses, but that drug states produced by Gallimine (a curareform drug with few effects on the central nervous system) and tetraethylammonium (a drug which produces a blockade of the autonomic nervous system) failed to acquire good response control. These results led Overton to doubt the idea that pentobarbital acquires response control via minor peripheral cues such as the blurring of vision. Noting also that pentobarbital acquired control of responses much more quickly than sensory cues, Overton theorized that pentobarbital and discriminative cues acquire response control via different mechanisms (Overton, 1964).

Overton (1967b) continued his research variation between different drugs concerning acquisition of response control. Overton trained rats to escape shock by running to one of three different goal boxes in a three-choice maze. A different goal box was "safe" for each of three drug states (phenobarbital, atropine, or saline). Overton reported that "atropine, phenobarbital and saline create three different states in the rat which may be used in control responses" (page 378). In other words, there was dissociation of learning between three drug states.

Overton (1968) researched perceptual factors as mediating mechanisms in state dependent learning. He designed a group of experiments to test the effects of increased foot shock, blinding, and varying

drug dosages upon the mechanism of dissociation. Overton reported that variations in foot shock did not mediate response control by pentobarbital ($F=1.65$ $df=2/15$). Overton concluded from this finding that variations in shock sensitivity (as induced by pentobarbital) are not a significant factor ($p < .001$) in mediating pentobarbital's control of differential responses. In the same article, Overton reported results of an experiment designed to determine the extent to which visual cues are a factor in state dependent learning. Rats were trained to turn one way under pentobarbital and the opposite way in the non-drug state. After training, the rats were blinded. Overton reported no noticable disruption of their performance. Overton concluded from these findings that visual perception is not a significant "cue" in the phenomenon of state dependent learning. In the final experiment of the series, Overton attempted to study the effects of varying drug dosages. He reported that control of differential responses was acquired as quickly between varying dosages of pentobarbital (20 mg/kg vs. 10 mg/kg) as it was between 10 mg/kg dosage and the non-drug state. He also reported previously (1964) that the larger dosage was more easily differentiated from the non-drug state than was the smaller dosage (Overton, 1968).

Overton (1966) reported on the effectiveness in producing dissociation of various depressant and atropine-like drugs. Overton reported that various depressant drugs (chloral hydrate, paraldhyde, secobarbital, sodium barbital, ambibarbital, chloralose and ether) mimic the effects of dissociation produced by pentobarbital. He also reported that rats could not learn differential responses between

two different depressant drugs. From these findings, Overton concluded that the depressant drugs studied produced dissociation via similar processes.

Overton (1966) also found that bemeguile sulphate (an antagonistic drug to pentobarbital) would eliminate the response learned in the drug (pentobarbital) state and produce behavior which was previously learned in the non-drug state. This finding raises questions about the relevance of changes in brain chemistry (i.e., levels of activation) to the phenomenon of state dependent learning. Overton also concluded that pentobarbital and atropine produce dissociation via different mechanisms, and that pentobarbital and atropine do not antagonize each other's dissociative effects. Overton also concluded that scopolamine and phenobarbital produce dissociative effects via different mechanisms, and that atropine and scopolamine produce identical dissociated states via the same mechanism. Overton concluded that atropine and other centrally acting anticholinergic drugs produce dissociation from both non-drug and depressant drug states, and that the anticholinergic drugs and depressant drugs produce dissociation via different mechanisms.

In studying the dissociative effects of other drugs, Overton (1966) concluded that chlorpromazine has no strong dissociative effect, nor does imipramine or physostigmine on T-maze learning. Erythroidine, a curareform drug used by Girden and Culler (1937) to produce dissociated learning in dogs, was not shown to mimic either pentobarbital or atropine, but the data were not statistically significant. Chloradiazepoxide (Librium) was shown to have

dissociative effects on T-maze learning. Overton's findings are significant in that by showing that different drugs produce dissociation via different mechanisms, he has shown that Girden's cortical/sub-cortical explanation of state dependent learning is inadequate.

Overton proposed two models of learning which help to explain his findings. The first model explains dissociation through the hypothesis that drug states serve as stimuli to receptor systems in the brain, and different drug states are responded to differently as are different stimuli. The second of Overton's models assumes that the chemical actions of the drugs change the characteristics of the cells of the brain that are altered as learning occurs. Hebb (1958) has theorized that in learning, structural changes in the synapse occur. Overton theorized that these structures are influenced by the effects of different drugs, and thus respond differently in different drug states (Overton, 1966).

Otis (1964) has also suggested that the internal drug state may serve as a stimulus to the animal. He stated, "an internal state induced by a drug may function like a stimulus; that is, it may acquire habit loadings, or associative connections to responses" (Otis, 1964, p. 1347). Pusakulich and Nielson (1972) researched neural thresholds in state dependent learning in cats. Pusakulich and Nielson found that as drug dosages were increased, neural thresholds in the state dependent learning response also increased. Pusakulich and Nielson concluded that thresholds were related to the cat's experience with the drug, rather than the pharmacological action of the drug <u>per se</u>. Pusakulich and Nielson found that alteration in drug

state away from the state of initial learning produces an increase in conditioning thresholds and sufficient alteration, causes a loss of CR. This report is in theoretical agreement with Overton's proposed model of state dependent learning.

Disruption of dissociated learning. Connelly, Connelly and Epps (1973) demonstrated disruption of state dependent learning by emotionally-important stimuli in a discrimination learning paradigm. Rats were trained to escape foot shock in a T-maze. They were trained to turn one direction while in the drug (15mg/kg chlordiazepoxide) state, and the opposite direction while in the non-drug (sterile water) state. For the transfer group, a high (10 kHz) tone was paired with foot shock in training in the drug state and a low (1 kHz) tone was paired with foot shock in training in the non-drug state. When tested with tones reversed; that is, high tone-non-drug state and low tone-drug state, the transfer group rats turned in accordance with the tone instead of the drug state. Connelly, et. al. concluded "That the tones acquired the aversive-motivational characteristics of foot shock and disrupted dissociated learning by mediating transfer" (p. 275). In other words, the emotional response (to the shock), when directed by a specific cue (the tones) was a more powerful determinant of behavior than were the different drug states.

Connelly, Connelly and Phifer (1975) demonstrated disruption of state dependent learning by emotionally-important stimuli. Rats were trained to escape shock in a T-maze. Rats were trained in either drug (40mg/kg chlordiazepoxide) state or non-drug (sterile water) state. A 1 kHz tone was paired with foot shock in training

and sounded in testing, although no shock was used in testing. Connelly, et. al. (1975) found that rats turned in the direction signaled by the tone regardless of drug state. In other words, the emotionally-important stimulus (tone) was more powerful than the drug state.

Alcohol and state dependent learning. Ethyl alcohol is one of the oldest intoxicants known to man. The chemical formula for alcohol is C_2H_5OH. Kalant (1971) stated that ethanol is made up of an -OH group linked to two carbon atoms.

Physiological effects of alcohol include a reduction in the amount of oxygen consumption in the brain and an inhibition in phosphate uptake by the brain. Grennell (1971) suggests that the main effect of alcohol in the brain is on the neuronal and synaptic membranes. Grennell also states that low concentrations of alcohol stimulate neuronal activity, while high concentrations of alcohol depress neuronal activity. These effects have great relevance to the area of state dependent learning, especially when considered in the light of the Overton models for explanation of state dependent learning (1966).

Problem

The problem was to discover the effects of foot shock (.65mA) paired with a tone (1kHz) on state dependent learning in rats in a T-maze escape learning task. This problem differed from the work of Connelly, et. al. (1975) in that ethanol was used to produce the drug state instead of chlordiazepoxide.

Hypothesis

The hypotheses of this study were: 1) There will be no statistically significant transfer of learning between drug states (ethanol vs. water) in the state dependent learning (no tone) groups. 2) There will be statistically significant transfer of learning between drug states (ethanol vs. water) in the transfer (tone) groups. The differences in transfer of learning between the state dependent learning and the transfer groups should be attributed to the tone's function as a mediator between drug states and cue to the emotional response of shock avoidance.

Significance of the study

The most obvious and potentially useful application of this type of study is in the area of drug addiction. Overton (1971) has observed that abused drugs are also drugs which produce state dependency.

Storm and Caird (1967) have demonstrated state dependent learning using alcohol in a serial verbal learning task. Also Storm and Smart (1965) have raised the possibility that dissociation could be a factor in the lack of success in alcoholic treatment programs. Noting that current treatment programs refuse to treat alcoholics while they are intoxicated, Storm and Smart (1965) suggest that it may be impossible for learning (therapy) to transfer from the sober to the intoxicated state. If this theory is correct, then the disruption of state dependent learning by emotion could cast light on more effective methods of treating drug addiction.

CHAPTER II

METHOD

Subjects

The subjects were sixty-four male hooded rats, eighty days of age, ordered from Maxfield Farms, Ohio. The rats were kept in individual cages and allowed free access to food and water. A light was kept on constantly in the cage room.

Apparatus

The apparatus used was a gray, wooden modified T-maze. The dimensions were as follows: width of all sections was 14 cm., length of all sections was 23 cm. The height of the start box was 28 cm., while the height of the goal boxes and choice section were 13 cm.

Guillotine doors were placed at the entrance of each goal box, and between the start box and the choice section. The doors to the goal boxes were covered with black curtains. The device was the same as the maze used by Connelly, et. al. (1975).

The maze contained a grid floor throughout which was electrified, except in the goal boxes, during training. A 0.65 mA shock was delivered by a Lafayette Master Shocker and Scrambler. A Lafayette 0.01-second timer was used to record response latencies.

The 1 kHz 600 mW tone was delivered through an unenclosed 13 cm. radio speaker placed 28 cm. behind the start section. A Heathkit Audio Generator (Model 16-72) and Scientific Power amplifier were used to deliver the tone.

Drugs

The drug used in this experiment was ethyl alcohol, 1000 mg/kg concentration. Distilled water was used to produce the non-drug (ND) state.

Procedure

Rats were given three days acclimation to the lab upon arrival. During this time they were kept in their home cages. On the fourth day, rats were given position preference trials. Rats were placed in the maze with both goal box doors open and the shock turned off. When the rats entered a goal box, they were removed to the home cage for fifteen seconds and placed in the maze again. The first three of five choices in the same direction was considered to be the rats' position preference.

Rats were weighed daily before injection to determine the volume of alcohol or water to be used. Body weight in grams was multiplied by a factor of 0.03 to determine the dosage in cc. For example, a rat weighing 300 grams was injected with 9.00 cc of liquid (300 x 0.03 = 9.00). Rats were injected intra-peritonealy (I.P.). After alcohol injections, rats were observed until they showed evidence of being drugged at which time training was begun. Time intervals between injection and drug effect varied with individual rats. Intervals between injection and running in non-drug rats were kept the same as intervals in the drugged rats for control purposes.

Rats were trained to escape foot shock in the modified T-maze. The rats were injected (with alcohol or sterile water), the time interval was observed, and then the rats were trained to turn in the direction opposite their position preference by a forced choice method. The rats were dropped onto the floor of the start box with the door to the correct goal box open and the door to the incorrect goal box closed. The rats received foot shock until they reached the correct goal box. As soon as the rats left the start box, the door between the start box and the choice section was closed.

Each rat received five massed training trials every day. Rats were trained to a criterion of eighteen of twenty correct choices. The first day of training was not counted toward criterion. After the rats reached criterion they were tested according to the patterns specified below.

Training was identical in both the state dependent learning and transfer groups, except that in the transfer groups, all rats were subjected to a 1 kHz tone on every training and every testing trial. The tone was sounded just before the rat was dropped onto the floor of the start box and ended when the rat entered the goal box. No state dependent learning groups were ever given the tone.

The groups for the study were: State-dependent learning groups (SDL); 1) SDL experimental group trained in the drug (D) state and tested according to the pattern ND-D-ND. . . 2) SDL experimental group trained in the non-drug (ND) state and tested according to the pattern D-ND-D. . . 3) SDL control group trained in the drug (D) state and tested according to the pattern D-D-D. . . 4) SDL

control group trained in the non-drug (ND) state and tested according to the pattern ND-ND-ND. . .: Transfer groups (T); 1) T experimental group trained in the drug (D) state and tested according to the pattern ND-D-ND. . . 2) T experimental group trained in the non-drug (ND) state and tested according to the pattern D-ND-D. . . 3) T control group trained in the drug (D) state and tested according to the pattern D-D-D. . . 4) T control group trained in the non-drug (ND) state and tested according to the pattern ND-ND-ND.

CHAPTER III

RESULTS

Results were analyzed according to the analysis of variance (ANOVA) found in Winer (1971). The two parameters of the ANOVA were the presence or absence of a tone and the drug state. The ANOVAs were: training, correct turns; training, median latencies; testing, correct turns; testing, median latencies. Sub-ANOVAs were also done. These were: training, correct turns for experimental groups; training, correct turns for control groups; training, median latencies for experimental groups; training, median latencies for control groups; testing, correct turns for experimental groups; testing, correct turns for control groups; testing, median latencies for experimental groups; testing, median latencies for control groups.

Results of the overall ANOVA for training, correct turns indicated that the drug states (D vs. ND) had a significant effect on performance ($p < .05$). The sub-ANOVAs for training, correct turns also indicated that drug state had a significant effect on performance in both the experimental and control groups ($p < .05$). Figures 1 and 2 indicate that the groups trained in the drug state did not learn as quickly as those trained in the non-drug state (see Appendix A). The main differences in performance occurred in the early stages of training. These differences may be due to the physiological effects of alcohol. The effects of the alcohol can be seen in the difference between the number of correct turns made on

day 1 by the drug groups as opposed to the non-drug groups. The groups trained in the drug state made 66 of 160 correct choices on day 1 compared to 94 of 160 for the groups trained in the non-drug state. First day performances of some of the groups trained in the drug state were very poor compared to the non-drug groups. For example, the D-T control group exhibited the worst performance of any group (14 of 40 correct choices), whereas the overall average for all 8 groups was 20 of 40 correct choices. All groups trained in the drug state made less than 20 correct choices on day 1, while all groups trained in the non drug state made 20 or more correct turns. The mean number of correct turns for the group trained in the drug state was 16.5, compared to 23.5 for groups trained in the non-drug state. This poor performance of the groups trained in the drug state helps to account for the significance of the overall interaction effect.

The overall interaction effect of the ANOVA for training, correct turns was found to be significant at the .05 level. This significance may be due to the poor performances of two of the groups during training. These groups were the T-D experimental group and the T-D control group (see Figures 1 and 2, Appendix A). It may be that the slower rate of learning shown by these two groups is responsible for the significance of the overall interaction effect.

All significance in the overall ANOVA of training, correct turns was the trial effect ($p < .001$). This significance can be attributed to learning. For example, on day 1 of training there were 170 of 320 correct turns for all groups. On day 2 this figure rose to 272 of 320 correct turns, and on day 3, there were 307 of 320

correct turns. The number of correct turns remained fairly consistant over the last three days of training.

The overall ANOVA for the latencies on training showed a significant trial effect ($p < .01$) and a significant interaction effect between the drug state and the trial effect ($p < .01$). Again, this difference may be attributed to the physiological effects of alcohol. The average of the mean median latencies for groups trained in the drug state was 14.44 seconds for day 1, compared to 6.14 seconds for the groups trained in the non drug state. The D-T experimental group had an average of the mean median latencies of 20.56 seconds for day 1 of training, and the D-SDL-control group had an average of the mean median latencies of 20.11 seconds for day 1 of training. These extreme results could be responsible for the significance of the overall interaction. The mean median latencies for days 3, 4 and 5 of training were more nearly equal. This was due to the rats' learning the task. As the results show (see figures 5 and 6, Appendix A), once the animals trained in the drug state learned the task, their performance was not greatly different from that of the animals trained in the non drug state.

The overall ANOVA for testing, correct turns showed that all three factors (tone vs. no tone, drug vs. non drug and trial effect) had significant effects ($p < .01$) on the results. The results as shown in figure 3 (see Appendix A) indicate that the two SDL groups' performances fell off sharply when they were tested in the drug state opposite their training drug state. The SDL experimental groups made only 47 of 80 correct choices when tested on the first day (in

the drug state opposite to training). The SDL control groups made 77 of 80 correct choices on the first day of testing. On day 3, the second day of testing in the drug state opposite to training, the SDL experimental groups made 38 of 80 correct choices. On day 3, the SDL control groups made 74 of 80 correct choices. On day 5, the third day of testing in the drug state opposite to training, the SDL experimental groups made 31 of 80 correct choices. On day 5, the SDL control groups made 71 of 80 correct choices. This decrease in performance on the part of the SDL experimental groups may be responsible for the significance of the overall interaction. The decrease may be due to the alternation of drug states in testing.

Contrary to the poor performance of the SDL experimental groups, the transfer (T) experimental groups maintained a relatively consistent level of performance throughout all five days of testing. This consistency can be attributed to the function of the tone as an emotional memory prompter which allowed learning to transfer across drug states.

The sub-ANOVA for the control groups showed no significant interactions except for the overall interaction. This significance may be due to poor performances by two of the groups on individual days. The ND-T-control group made 29 of 40 correct choices on day 3, compared to an average over all five days of 35.2. Also, the ND-SDL-control group made 31 of 40 correct choices on day 5, compared to an average over five days of 35.4. The best average over five days was 38.6 of 40 correct choices for the D-SDL-control group, while the worst average was 35.2 for the ND-T-control group. These individual variations could account for the significance of the

overall interaction effect.

In the sub-ANOVA for the two experimental groups, the presence or absence of the tone was significant at the .001 level. This greater level of significance shows more convincingly the importance of the tone as a memory prompter because this ANOVA deals only with the experimental groups. The two T experimental groups made a combined total of 358 of 400 correct choices for the five days of testing. The two SDL experimental groups made a combined total of 253 of 400 c orrect choices. These results show the value of the tone in helping the rats remember the correct choice.

The results of the ANOVAs for testing, median latencies were in agreement with the results of the ANOVAs for correct turns in testing. That is, they have shown the significance of the tone as a variable ($p < .01$).

The overall ANOVA also showed that variation in drug states and a combination of the tone and drug state variables were significant ($p < .05$). The results show a significant ($p < .005$, see Table XI, Appendix B) increase in latencies in the SDL groups when they were tested in the drug state opposite their training drug state (see Figure 7, Appendix A).

The average of the mean median latencies for the SDL experimental groups tested in the state opposite training was 25.41 seconds. The average of the mean median latencies for the same groups tested in the training drug state was 4.51 seconds.

The sub-ANOVA using only the experimental groups showed that those groups which heard the tone performed significantly better ($p < .01$)

than those who did not hear the tone. The average of the mean median latencies for the experimental groups which did not hear the tone (D-SDL and ND-SDL) was 17.15 seconds. The average of the mean median latencies for the experimental groups which did hear the tone (D-T and ND-T) was 5.01 seconds. Also, the variation between the individual days of testing in the experimental groups was significant at the .001 level. The interaction between the tone variable and the individual day variation was significant at the .05 level. The sub-ANOVA for the control groups showed no statistical significance. This would indicate that the significance of the interactions for the experimental groups was due to the alternation in drug states.

The overall interaction effect for testing median latencies was found to be significant at the .05 level. This significance may be due to the alternation in the drug states of the experimental groups (see Figure 7, Appendix A).

CHAPTER IV

DISCUSSION

Two results of this study support the hypothesis. The first of them is the significantly poorer performance of the SDL groups when tested in the drug state opposite their training drug state. Both correct turn and latency performance were adversely affected by introduction of the opposite drug state. The second result is the consistent performance of the T groups when tested in the drug state opposite of their training drug state. The only difference between the T groups and the SDL groups was the presence of a tone. Therefore, the tone must have been the factor which caused the T groups to maintain their level of performance despite the introduction of a drug state opposite to the training drug state. It is hypothesized that the tone served as an emotional memory prompter allowing learning to transfer across drug states. This explanation was previously given by Connelly, et. al. (1975).

Obviously, the rats quickly developed a fear of foot shock when being trained. This emotion served as a motivater to learn and perform the required task. However, when the SDL rats were tested in the drug state opposite their training drug state, the drug state "barrier" prevented them from constructively channeling their emotion into a successful performance. The SDL rats could not perform correctly because they had no specific stimulus to channel their emotion. On the other hand, the T group rats began to associate their emotion with the tone. The tone directed their emotion toward constructive

action because it was specific enough to transfer across the drug state "barrier" and serve as a memory prompter.

The overall interaction effect for training, correct turns was significant at the .05 level (see Table 1, Appendix B). This was probably due to the slower rate of learning displayed by two of the groups trained in the drug state (see Figures 1 and 2, Appendix A). The rate of learning in training did not effect the results in testing because all groups were trained to the same criterion. Also, the groups which showed a slower learning rate in testing (T-D experimental and T-D control) were two of the three best performing groups in testing (see Figures 3 and 4, Appendix A). The fact that the slow learning groups reversed their performances in testing is evidence that the overall interaction effect in training did not influence the results of testing.

Both of the overall interaction effects for testing were significant. The correct turn overall interaction effect was significant at the .01 level, while the latency interaction effect was significant at the .05 level (see Tables 7 and 10, Appendix B). These results were significant due to the extremely poor performance of the SDL experimental groups in testing in Days 2 and 4 (see Figures 3 and 7, Appendix A). In other words, these groups demonstrated state dependency while the other groups did not. This state dependency accounts for the significance of the overall interaction effects.

The one methodological problem worth noting concerned the wide variations in the time it took the alcohol to effect the rats. Some rats took up to an hour to reach a sufficient level of intoxication

while other rats became intoxicated in one minute or less after injection. This variation seemed to be related to the depth of the injection. If the injection was just under the skin, the interval between injection and intixication was from 15-min. to 1-hour. However, if the injection was made deeply enough, intoxication was very rapid. This discrepancy was alleviated by making sure the injections were always of equal depth.

Logical extensions of the study could include similar studies run with progressively less shock and less variation in stimuli between the SDL and T groups. In this way, perhaps researchers could vary the strength of the stimuli and therefore indirectly vary the strength of the emotion needed before transfer of learning across drug states could occur.

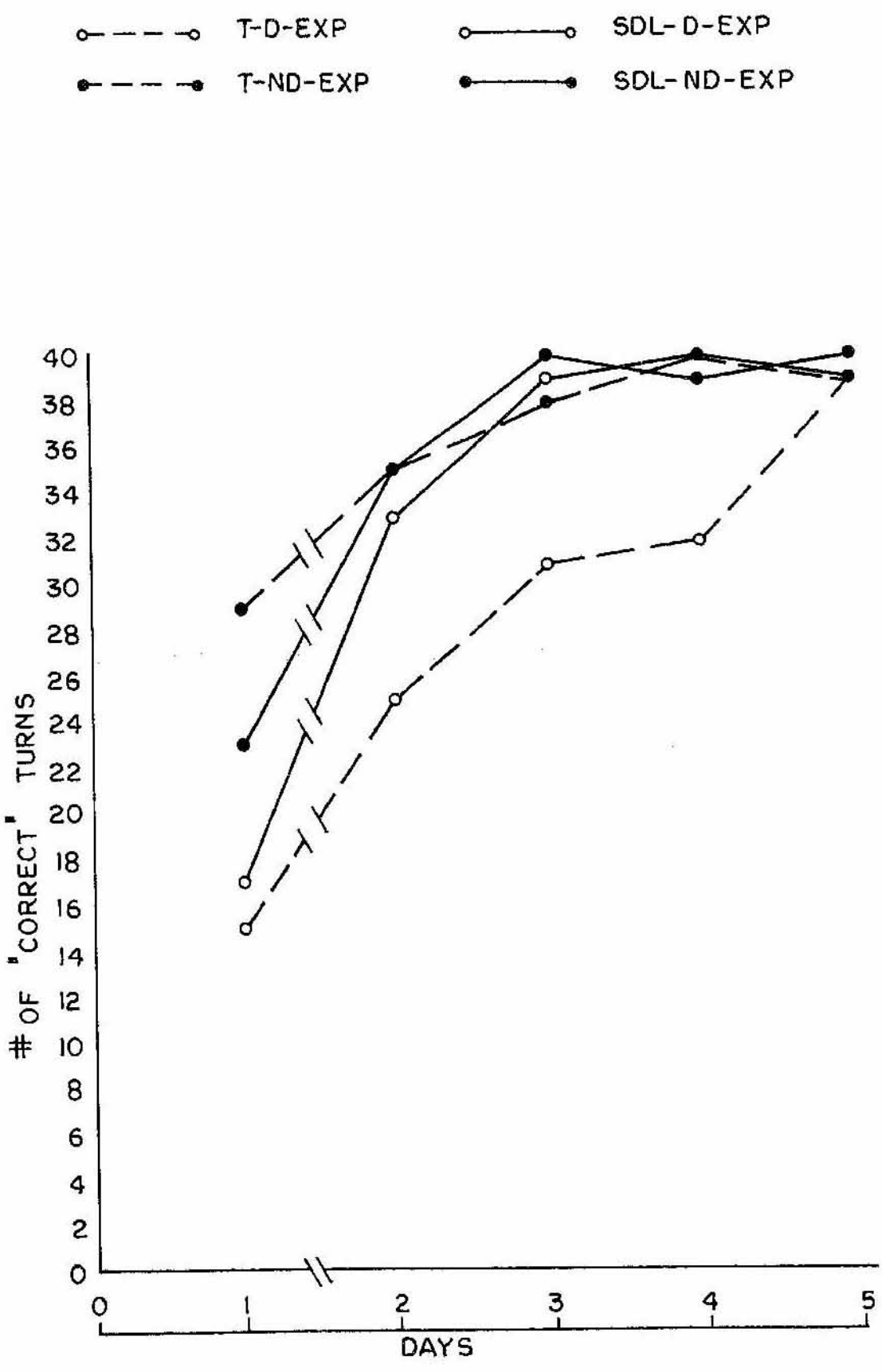
The greatest potential application of the findings of the study is in the area of alcoholism treatment. State dependency is one possible reason for the failure of current alcoholism treatment programs. The alcoholic receives all his therapy when sober, and therefore has no transfer of learning from the sober state to the intoxicated state. Therefore, the alcoholic gets no benefit from his therapy while he is intoxicated. Perhaps most important of all is the fact that the alcoholic has no aversive stimuli that he can transfer from the intoxicated state to the sober state. Therefore, he has no reason to stop getting drunk because he can remember nothing unpleasant that happens while he is drunk. If he were presented with an emotionally important stimulus while intoxicated, and if transfer of learning across drug states could be made to occur, then the alcoholic would have a reason not to drink which he could remember in

the sober state. This added motivation could be helpful in the treatment of alcoholism.

APPENDICES

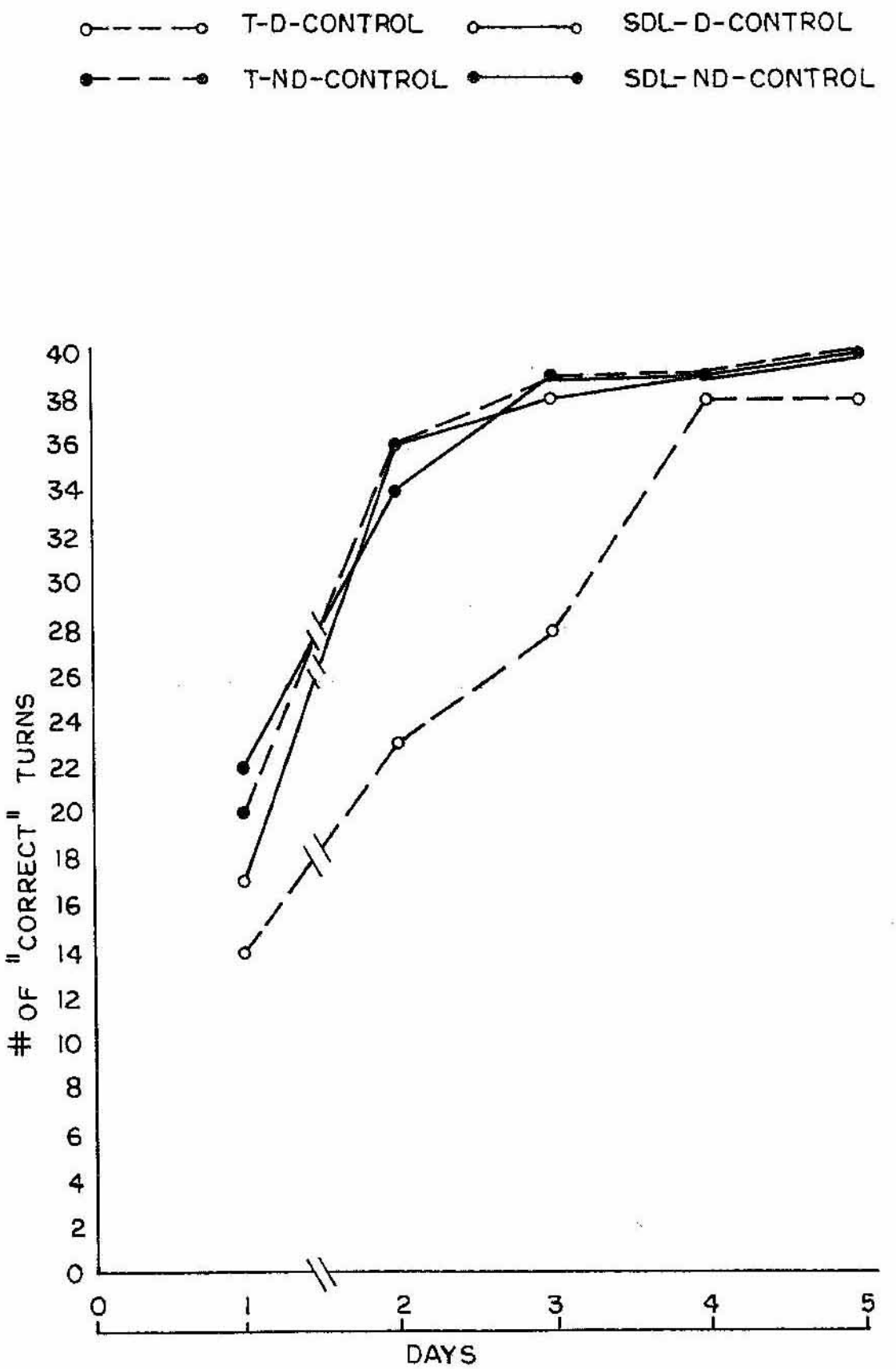
APPENDIX A

Figure 1 - Number of correct turns for the first and last 4 days of training for the experimental groups


T-D-EXP
SDL-D-EXP
T-ND-EXP
SDL-ND-EXP
OF 'CORRECT' TURNS
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
38
40
0
1
2
3
4
5
DAYS

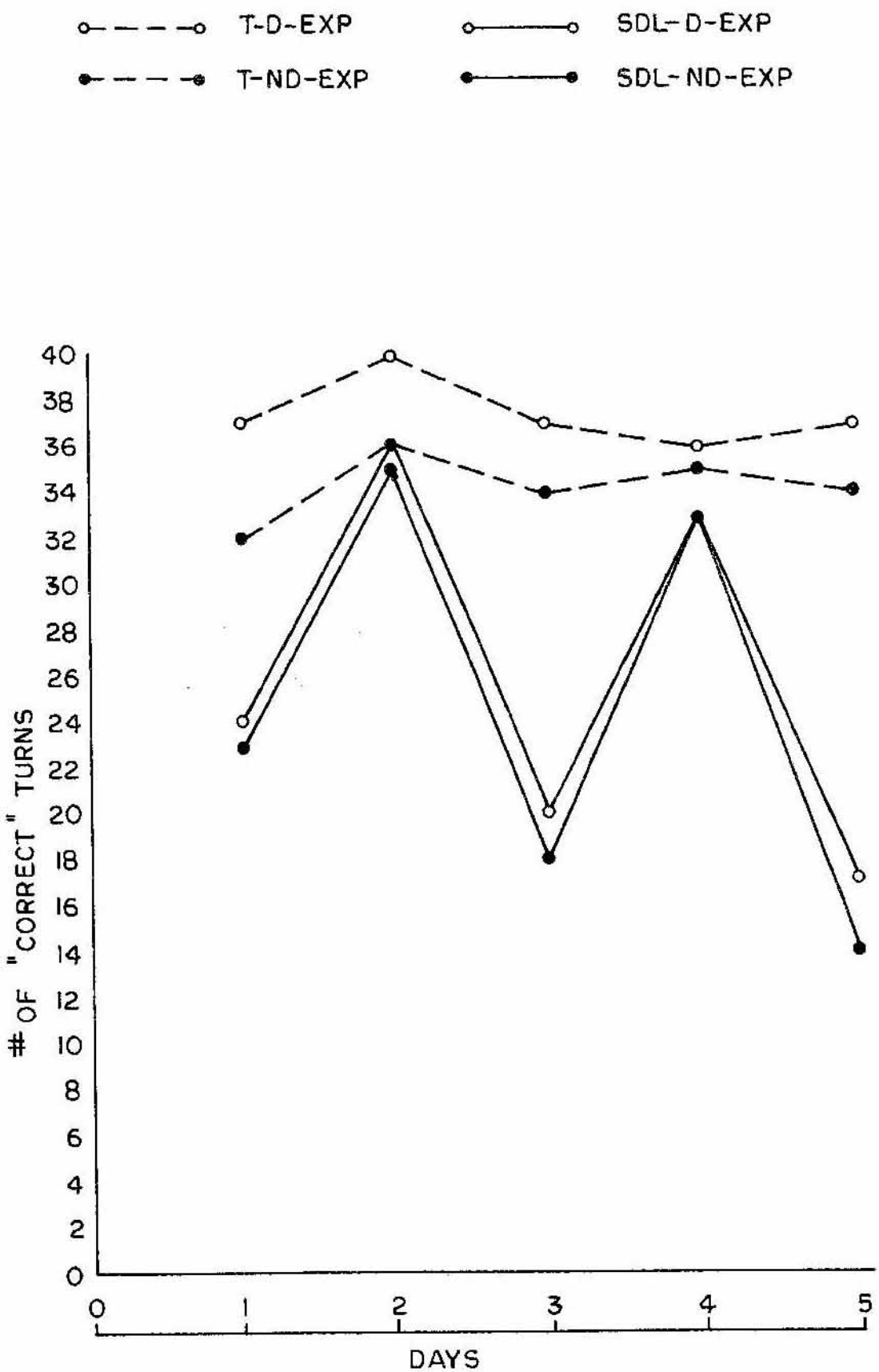
APPENDIX A

Figure 2 - Number of correct turns for the first and last 4 days of training for the control groups.


T-D-CONTROL
SDL-D-CONTROL
T-ND-CONTROL
SDL-ND-CONTROL
OF "CORRECT" TURNS
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
38
40
0
1
2
3
4
5
DAYS

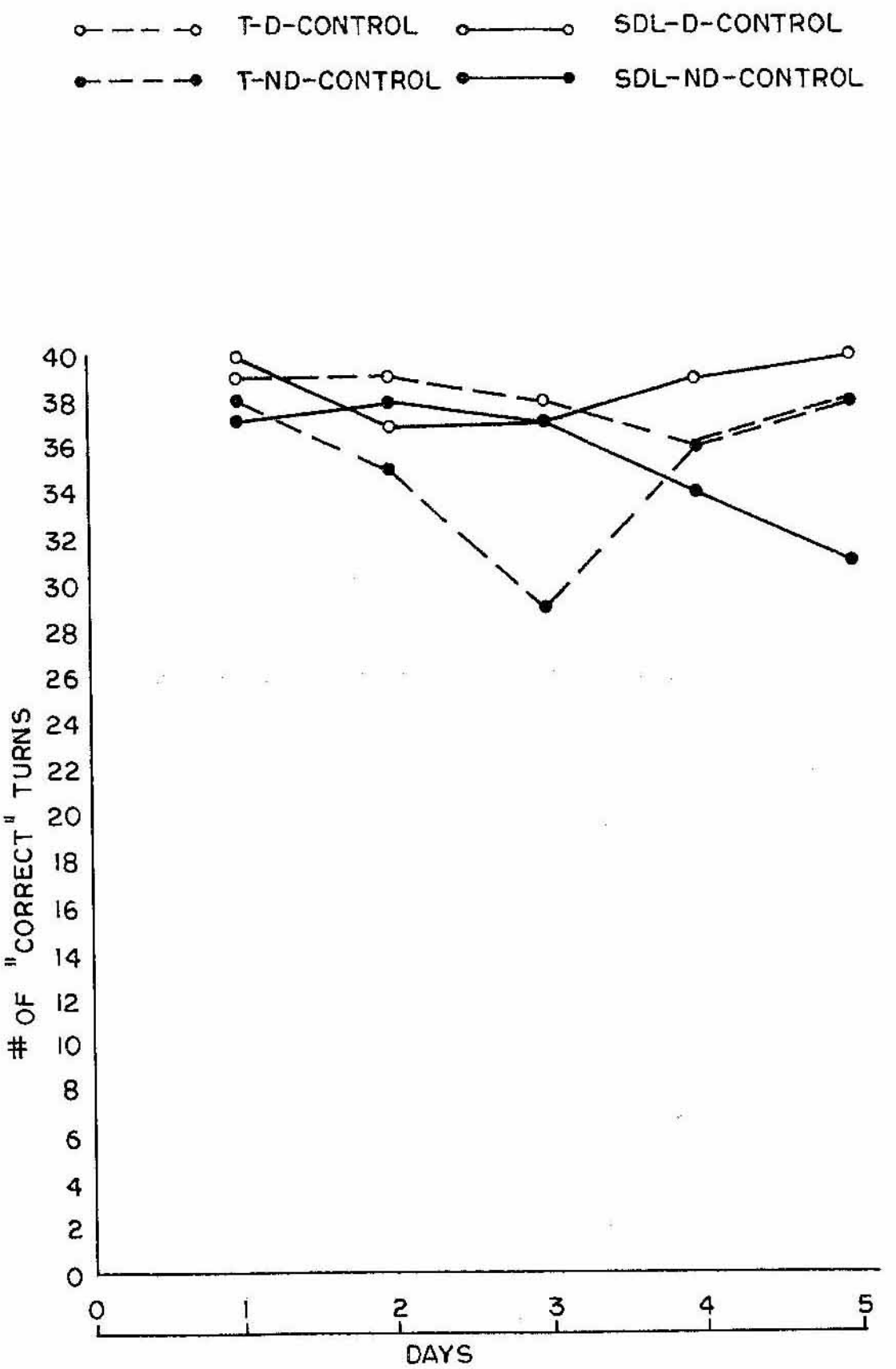
APPENDIX A

Figure 3 - Number of correct turns for the five days of testing for the experimental groups.


T-D-EXP
SDL-D-EXP
T-ND-EXP
SDL-ND-EXP
OF "CORRECT" TURNS
40
38
36
34
32
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
0
1
2
3
4
5
DAYS

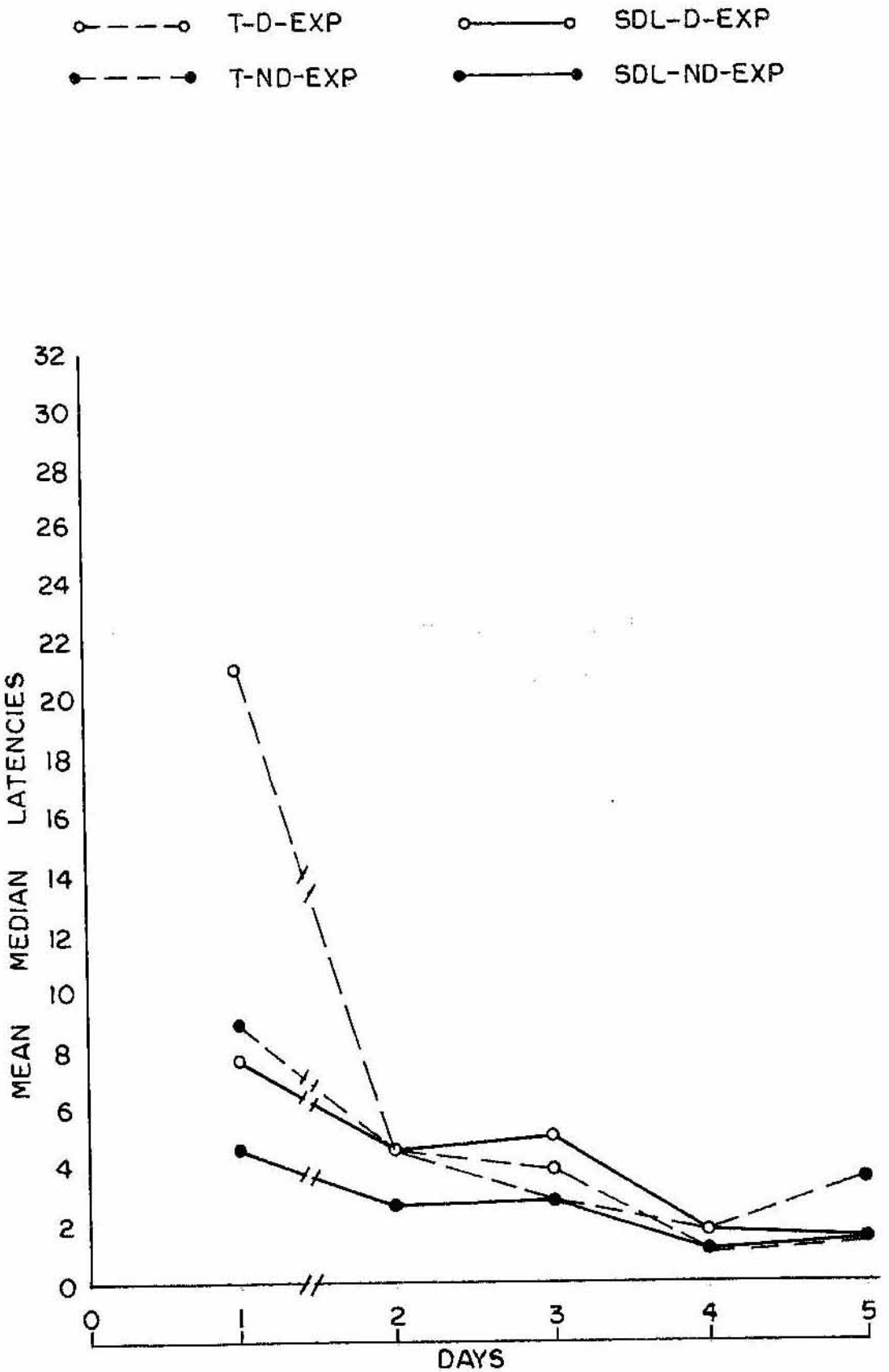
APPENDIX A

Figure 4 - Number of correct turns for the five days of testing for the control groups.


T-D-CONTROL
SDL-D-CONTROL
T-ND-CONTROL
SDL-ND-CONTROL
OF "CORRECT" TURNS
40
38
36
34
32
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
0
1
2
3
4
5
DAYS

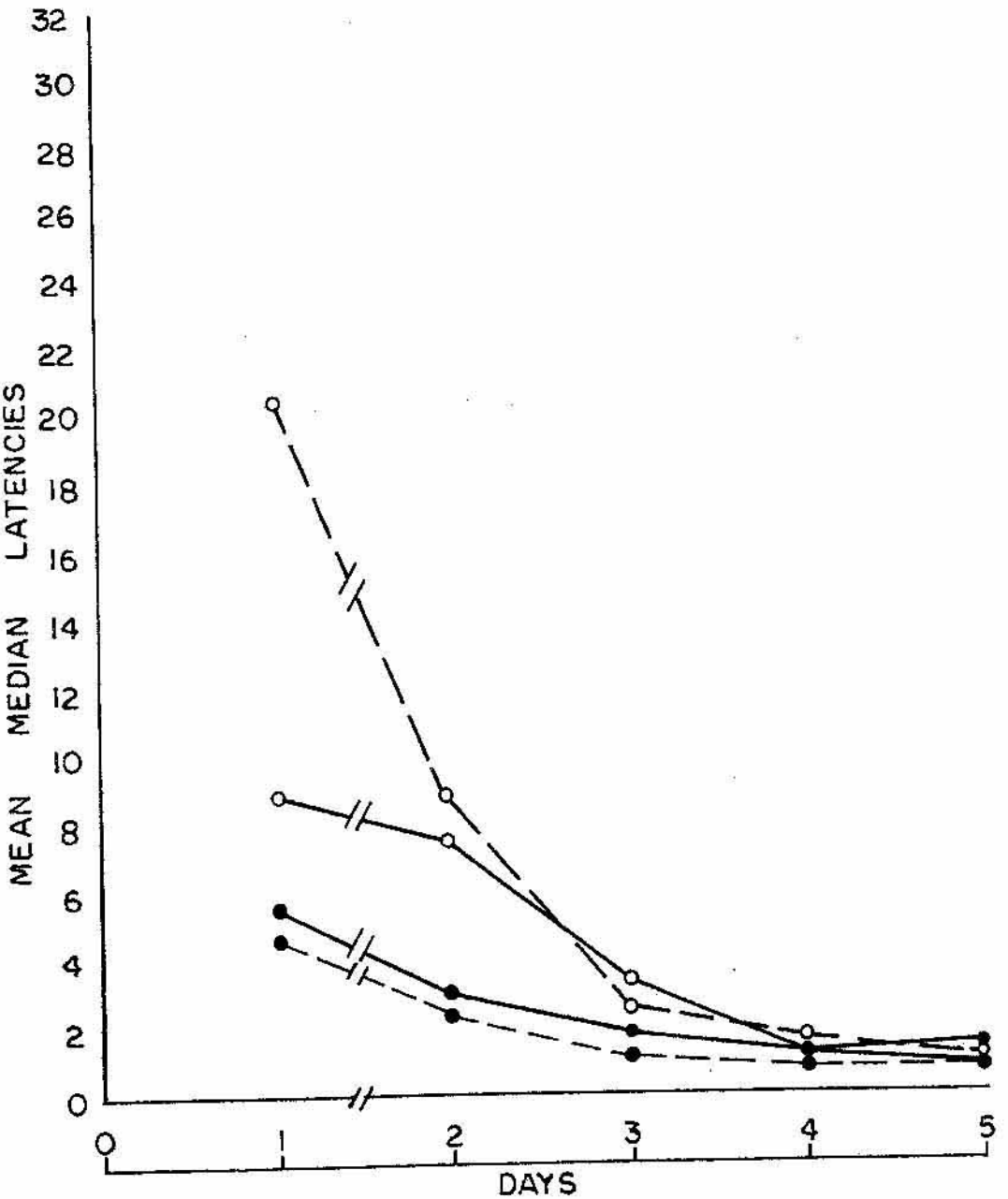
APPENDIX A

Figure 5 - Means of the median latencies for the first and last 4 days of training for the experimental groups.


T-D-EXP
SDL-D-EXP
T-ND-EXP
SDL-ND-EXP
MEAN MEDIAN LATENCIES
32
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
0
1
2
3
4
5
DAYS

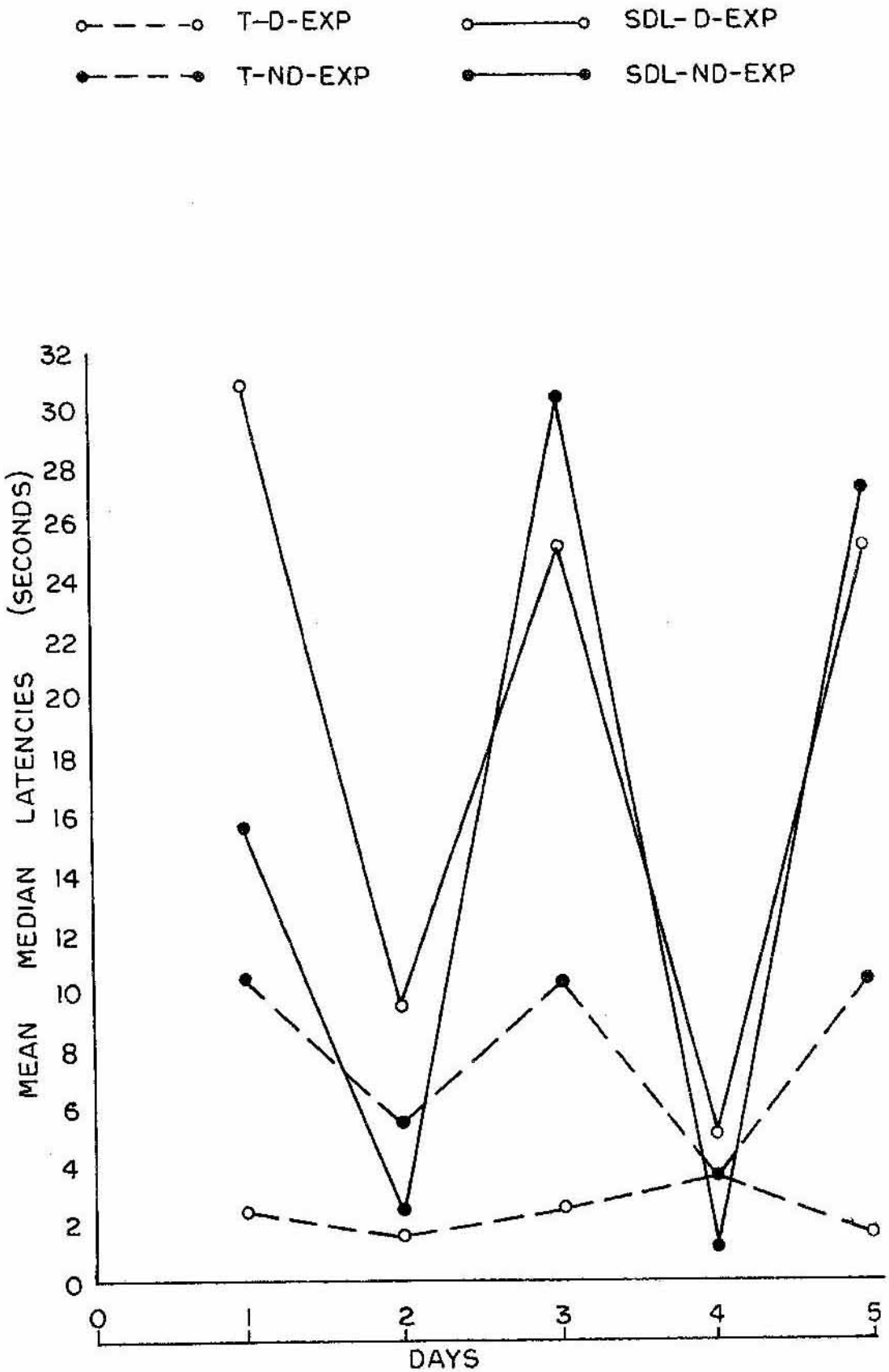
APPENDIX A

Figure 6 ~ Means of the median latencies for the first and last 4 days of training for the control groups.


T-D-CONTROL
SDL-D-CONTROL
T-ND-CONTROL
SDL-ND-CONTROL
MEAN MEDIAN LATENCIES
32
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
0
1
2
3
4
5
DAYS

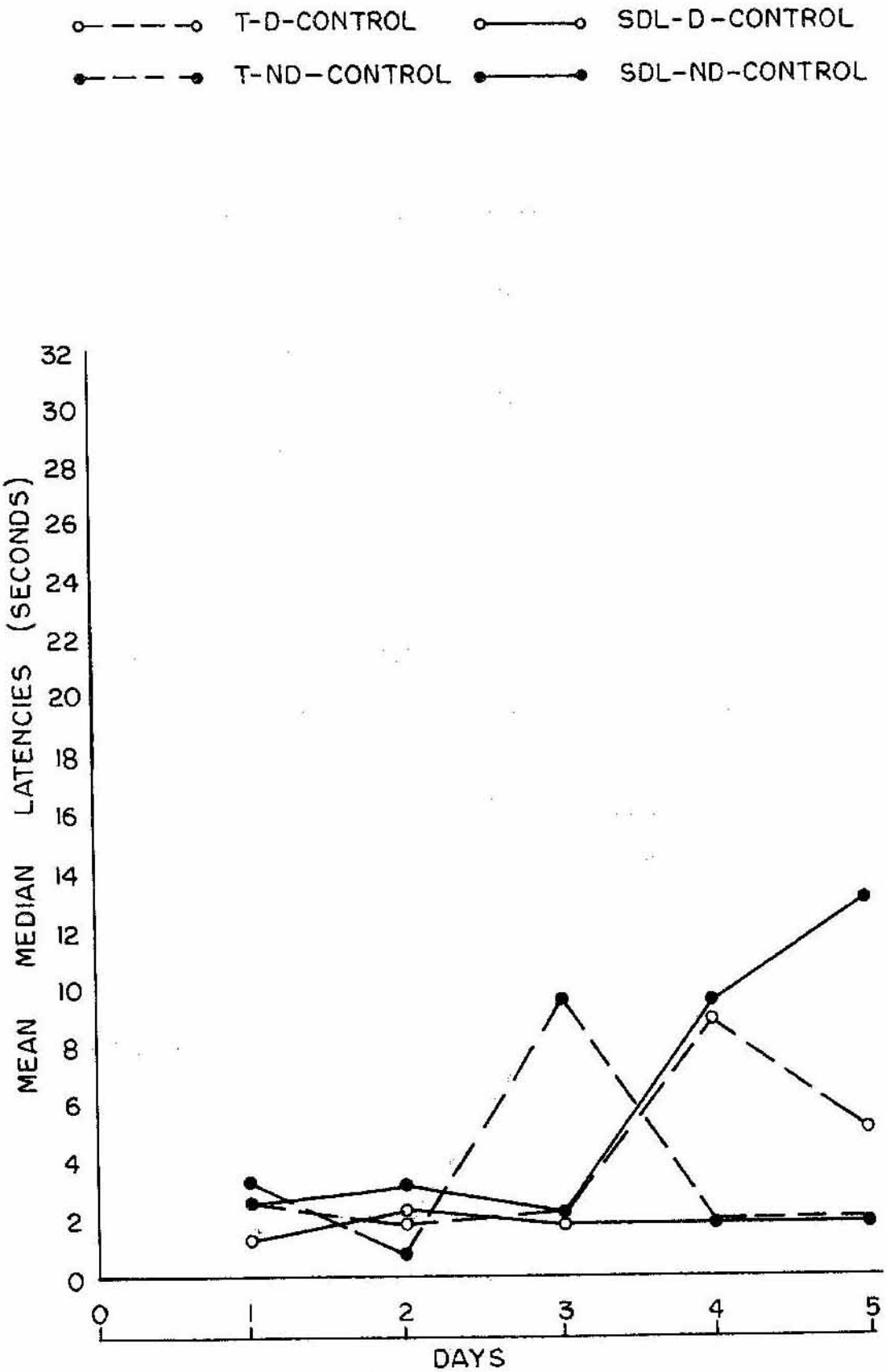
APPENDIX A

Figure 7 - Means of the median latencies for the five days of testing for the experimental groups.


T-D-EXP
SDL-D-EXP
T-ND-EXP
SDL-ND-EXP
MEAN MEDIAN LATENCIES (SECONDS)
32
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
0
1
2
3
4
5
DAYS

APPENDIX A

Figure 8 - Means of the median latencies for the five days of testing for the control groups.


T-D-CONTROL
SDL-D-CONTROL
T-ND-CONTROL
SDL-ND-CONTROL
MEAN MEDIAN LATENCIES (SECONDS)
32
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
0
1
2
3
4
5
DAYS

APPENDIX B

TABLE I

TRAINING, CORRECT TURNS, ALL GROUPS

Source	SS	df	MS	F	
Between	43.5	63			
A	0.3	1	0.3		
B	6.6	3	2.2	3.49	($p < .05$)
AB	1.3	3	.43		
Sub w. groups /error (between)/	35.3	56	.63		
Within Subjects	389.2	256			
C	274.0	4	68.5	155.68	($p < .001$)
AC	0.2	4	.05		
BC	5.9	12	.49	1.11	
ABC	10.4	12	.87	1.98	($p < .05$)
Cx Subgroups /error (within)/					

Note: A - Tone vs. No tone

B - D vs. ND

C - Days

TABLE II

TRAINING, CORRECT TURNS, EXPERIMENTAL GROUPS

Source	SS	df	MS	F	
Between	21.78	31			
A	0	1	0		
B	3.03	1	3.03	4.46	($p < .05$)
AB	0.4	1	0.4		
Sub w. groups /error (between)/	19.15	28	0.68		
Within	167.2	128			
C	115.41	4	28.85	75.92	($p < .001$)
AC	0.62	4	0.16		
BC	6.59	4	1.65	4.34	($p < .01$)
ABC	2.23	4	0.56	1.47	
Cx Sub w. groups /error (within)/	42.35	112	0.38		

Note: A - Tone vs. No tone

B - D vs. ND

C - Days

TABLE III

TRAINING CORRECT TURNS, CONTROL GROUPS

Source	SS	df	MS	F	
Between	19.9	31			
A	0.62	1	0.62	1.07	
B	2.5	1	2.5	4.31	($p < .05$)
AB	0.63	1	0.63	1.09	
Sub w. groups /error (between)/	16.15	28	0.58		
Within S's	222	128			
C	161.21	4	40.30	80.60	($p < .001$)
AC	0.7	4	0.18		
BC	2.32	4	0.58	1.16	
ABC	1.42	4	0.36		
Cx Sub w. groups /error (within)/	56.35	112	0.50		

Note: A - Tone vs. No tone

B - D vs. ND

C - Days

TABLE IV

MEAN MEDIAN LATENCIES, TRAINING, ALL GROUPS

Source	SS	df	MS	F	
Between	4734.07	63			
A	31.18	1	31.18		
B	503.8	3	167.93	2.33	
AB	130.33	3	43.44		
Sub w. groups /error (between)/	4041.76	56	72.17		
Within	16955.92	256			
C	4620.49	4	1155.12	24.66	($p < .01$)
AC	30.44	4	7.61		
BC	1395.73	12	116.31	2.48	($p < .01$)
ABC	425.61	12	35.47		
Cx Subgroups /error (within)/	10493.65	224	46.85		

Note: A - Tone vs. No tone

B - D vs. ND

C - Days

TABLE V

MEAN MEDIAN LATENCIES, TRAINING, EXPERIMENTAL GROUPS

Source	SS	df	MS	F	
Between	2857.79	31			
A	144.19	1	144.19	1.59	
B	172.87	1	172.87	1.90	
AB	0.43	1	0.43		
Sub w. groups /error (between)/	2540.3	28	90.73		
Within S's	9373.76	128			
C	2574.71	4	643.68	12.17	($p < .001$)
AC	116.71	4	29.18		
BS	747.55	4	186.89	3.53	($p < .01$)
ABC	9.74	4	2.44		
Cx Subgroups /error (within)/	5925.05	112	52.90		

Note: A - Tone vs. No tone

B - D vs. ND

C - Days

TABLE VI

MEAN MEDIAN LATENCIES, TRAINING, CONTROL GROUPS

Source	SS	df	MS	F	
Between	1857.81	31			
A	16.89	1	16.89		
B	339.46	1	339.46	6.33	($p < .05$)
AB	0	1	0		
Sub w. groups /error (between)/	1501.46	28	53.62		
Within S's	7582.17	128			
C	2068.09	4	517.03	12.68	($p < .001$)
AC	172.33	4	43.08	10.56	($p < .001$)
BC	615.87	4	153.97	3.77	($p < .01$)
ABC	157.3	4	39.33		
Cx Sub w. groups /error (within)/	4568.58	112	40.79		

Note: A - Tone vs. No tone

B - D vs. ND

C - Days

TABLE VII

TESTING, CORRECT TURNS, ALL GROUPS

Source	SS	df	MS	F	
Between	296.75	63			
A	32.51	1	32.51	10.80	($p < .01$)
B	57.27	3	19.09	6.34	($p < .01$)
AB	38.47	3	12.82	4.26	($p < .01$)
Sub w. groups /error (between)/	168.5	56	3.01		
Within	258.8	256			
C	25.33	4	6.33	8.44	($p < .01$)
AC	18.59	4	4.65	6.2	($p < .01$)
BC	23.83	12	1.99	2.65	($p < .01$)
ABC	23.3	12	1.94	2.59	($p < .01$)
Cx subgroups /error (within)/	167.75	224	0.75		

Note: A - Tone vs. No tone

B - D-D-D vs. ND-ND-ND vs. D-ND-D

C - Days

TABLE VIII

TESTING CORRECT TURNS, EXPERIMENTAL GROUPS

Source	SS	df	MS	F	
Between	190.3	31			
A	70.23	1	70.23	16.96	($p < .001$)
B	3.6	1	3.6		
AB	0.72	1	0.72		
Sub w. groups /error (between)/	115.85	28	4.14		
Within	190.8	128			
C	44.66	4	11.17	11.06	($p < .001$)
AC	32.59	4	8.15	8.07	($p < .001$)
BC	0.59	4	0.15		
ABC	0.31	4	0.08		
Cx Sub. w groups /error (within)/	112.65	112	1.01		

Note: A - Tone vs. No tone

B - D-ND-D vs. ND-D-ND

C - Days

TABLE IX

TESTING CORRECT TURNS, CONTROL GROUPS

Source	SS	df	MS	F	
Between	58.4	31			
A	0.1	1	0.1		
B	5.62	1	5.62	2.98	
AB	0.03	1	0.03		
Sub w. groups /error (between)/	52.65	28	1.88		
Within	68.0	128			
C	2.9	4	0.73	1.49	
AC	2.28	4	0.57	1.16	
BC	1.01	4	0.25		
ABC	6.71	4	1.68	3.43	($p < .05$)
Cx Sub w. groups /error (within)/	55.1	112	.49		

Note: A - Tone vs. No tone

B - D vs. ND

C - Days

TABLE X

MEAN MEDIAN LATENCIES, TESTING, ALL GROUPS

Source	SS	df	MS	F	
Between	34953.68	63			
A	2992.96	1	2992.96	7.13	($p < .01$)
B	4445.04	3	1481.68	3.53	($p < .05$)
AB	4006.31	3	1335.44	3.18	($p < .05$)
Sub w. groups /error (between)/	23509.37	56	419.81		
Within	40764.34	256			
C	3017.69	4	754.42	5.80	($p < .01$)
AC	1596.74	4	399.19	3.07	($p < .05$)
BC	3767.0	12	313.92	2.41	($p < .01$)
ABC	3254.3	12	271.19	2.08	($p < .05$)
Cx sub groups /error (within)/	29128.61	224	130.04		

Note: A - Tone vs. No tone

B - D-D-D vs. ND-ND-ND vs. D-ND-D

C - Days

TABLE XI

MEAN MEDIAN LATENCIES, TESTING, EXPERIMENTAL GROUPS

Source	SS	df	MS	F	
Between	25393.69	31			
A	5886.81	1	5886.81	8.87	($p < .01$)
B	45.58	1	45.58		
AB	881.39	1	881.39	1.33	
S's w. groups /error (between)/	18579.91	28	663.57		
Within	30586.43	128			
C	5549.91	4	1387.48	7.61	($p < .001$)
AC	3264.64	4	816.16	4.48	($p < .005$)
BC	746.71	4	186.68	1.02	
ABC	617.65	4	154.41		
Cx Sub w. groups /error (within)/	20407.52	112	182.21		

Note: A - Tone vs. No tone

B - D-ND-D vs. ND-D-ND

C - Days

TABLE XII

MEAN MEDIAN LATENCIES, TESTING, CONTROL GROUPS

Source	SS	df	MS	F	
Between	5282.33	31			
A	0.42	1	0.42		
B	121.74	1	121.74		
AB	230.68	1	230.68	1.31	
Sub w groups /error (between)/	4929.49	28	176.05		
Within sub's	10181.69	128			
C	358.17	4	89.54	1.15	($p < .05$)
AC	253.5	4	63.88		
BC	129.92	4	32.48		
ABC	715.23	4	178.81	2.29	
Cx sub w. groups /error (within)/	8724.87	112	77.90		

Note: A - Tone vs. No tone

B - D vs. ND

C - Days

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