43463

National Library of Canada / Bibliothèque nationale du Canada

CANADIAN THESES ON MICROFICHE / THÈSES CANADIENNES SUR MICROFICHE

NAME OF AUTHOR/NOM DE L'AUTEUR Arthur A. Leccese

TITLE OF THESIS/TITRE DE LA THÈSE Performance facilitation with formal structure: State directions; facilitation of consolidation at local level?

UNIVERSITY/UNIVERSITÉ University of Alberta

DEGREE FOR WHICH THESIS WAS PRESENTED/GRADE POUR LEQUEL CETTE THÈSE FUT PRÉSENTÉE Master of Science

YEAR THIS DEGREE CONFERRED/ANNÉE D'OBTENTION DE CE GRADE 1974

NAME OF SUPERVISOR/NOM DU DIRECTEUR DE THÈSE Dr. Ying Grant

Permission is hereby granted to the NATIONAL LIBRARY OF CANADA to microfilm this thesis and to lend or sell copies of the film.

The author reserves other publication rights, and neither the thesis nor extensive extracts from it may be printed or otherwise reproduced without the author's written permission.

L'autorisation est, par la présente, accordée à la BIBLIOTHÈQUE NATIONALE DU CANADA de microfilmer cette thèse et de prêter ou de vendre des exemplaires du film.

L'auteur se réserve les autres droits de publication; ni la thèse ni de longs extraits de celle-ci ne doivent être imprimés ou autrement reproduits sans l'autorisation écrite de l'auteur.

DATED/DATÉ June 25/1979 SIGNED/SIGNÉ Arthur A. Leccese

PERMANENT ADDRESS/RÉSIDENCE FIXE 7731 - 28 Avenue
Kenosha, Wisconsin, USA
53140

NL-91 (3-74)

National Library of Canada

Cataloguing Branch
Canadian Theses Division

Ottawa, Canada
K1A 0N4

Bibliothèque nationale du Canada

Direction du catalogage
Division des thèses canadiennes

NOTICE

The quality of this microfiche is heavily dependent upon the quality of the original thesis submitted for microfilming. Every effort has been made to ensure the highest quality of reproduction possible.

If pages are missing, contact the university which granted the degree.

Some pages may have indistinct print especially if the original pages were typed with a poor typewriter ribbon or if the university sent us a poor photocopy.

Previously copyrighted materials (journal articles, published tests, etc.) are not filmed.

Reproduction in full or in part of this film is governed by the Canadian Copyright Act, R.S.C. 1970, c. C-30. Please read the authorization forms which accompany this thesis.

THIS DISSERTATION
HAS BEEN MICROFILMED
EXACTLY AS RECEIVED

AVIS

La qualité de cette microfiche dépend grandement de la qualité de la thèse soumise au microfilmage. Nous avons tout fait pour assurer une qualité supérieure de reproduction.

S'il manque des pages, veuillez communiquer avec l'université qui a conféré le grade.

La qualité d'impression de certaines pages peut laisser à désirer, surtout si les pages originales ont été dactylographiées à l'aide d'un ruban usé ou si l'université nous a fait parvenir une photocopie de mauvaise qualité.

Les documents qui font déjà l'objet d'un droit d'auteur (articles de revue, examens publiés, etc.) ne sont pas microfilmés.

La reproduction, même partielle, de ce microfilm est soumise à la Loi canadienne sur le droit d'auteur, SRC 1970, c. C-30. Veuillez prendre connaissance des formules d'autorisation qui accompagnent cette thèse.

LA THÈSE A ÉTÉ
MICROFILMÉE TELLE QUE
NOUS L'AVONS REÇUE

NL-339 (3/77)

THE UNIVERSITY OF ALBERTA

PERFORMANCE FACILITATION WITH POSTTRIAL STRYCHNINE SULFATE INJECTIONS: FACILITATION OF CONSOLIDATION OR RETRIEVAL?

by

ARTHUR P. LECCESE

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND RESEARCH IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE

DEPARTMENT OF PSYCHOLOGY

EDMONTON, ALBERTA

THE UNIVERSITY OF ALBERTA

FACULTY OF GRADUATE STUDIES AND RESEARCH

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research, for acceptance, a thesis entitled "Performance facilitation with posttrial strychnine sulfate injections; Facilitation of consolidation or retrieval?" submitted by Arthur P. Leccese in partial fulfilment of the requirement for the degree of Master of Science.

.....

Supervisor

Roc L. Malley

.....

.....

Date. Nov. 11, 1979

Abstract

Time-dependent retrograde facilitation of retention with strychnine sulfate can be interpreted either in terms Spear's (1971, 1973) attribute-retrieval model of animal memory or in terms of Dawson and McGaugh's (1973) memory consolidation hypothesis. An experiment was conducted as a direct test between these explanations. In two preliminary experiments it was found that (a) a 1.50 mg/kg dose of strychnine sulfate was a facilitative dose for male Sprague-Dawley rats and (b) rats were capable of performing a discriminative choice task in a T-maze on the basis of cues provided by pretrial injections of strychnine sulfate or saline. Experiment III revealed that an immediately posttrial injection of strychnine sulfate facilitated retention on a test given seven days later only when the strychning sulfate state was reinstated at the time of test. This finding is consistent with a retrieval interpretation of the facilitative effect of posttrial injections of strychnine sulfate and inconsistent with a consolidation interpretation. It was concluded that (a) a retrieval account was best able to explain time-dependent retrograde facilitation with strychnine sulfate and (b) no study has unambiguously demonstrated that strychnine sulfate enhances memory consolidation.

ACKNOWLEDGMENTS

I gratefully acknowledge the help and guidance provided by Dr. Douglas Grant in the funding, design, execution, and preparation of the manuscript for the present experiments. I also thank Dr. Roc Walley for aiding in revision of this manuscript. Finally, I thank my wife, Linda, for her help in the execution of the experiment and for providing physical and moral support for the duration.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

Performance Facilitation with Posttrial Strychnine Sulfate Injections; Facilitation of Consolidation or Retrieval?

Since Lashley's (1917) original demonstration, numerous studies have found that performance by rats on a wide variety of tasks can be enhanced by injections of strychnine sulfate (Cooper & Krass, 1963; Greenough & [illegible], 1965; Hudspeth, 1964; Krivanek & Hunt, 1967; McGaugh & Thomson, 1962; McGaugh, Thomson, Westbrook & Hudspeth, 1962; Petrinovich, 1963, 1967) as well as other central nervous system stimulants (see McGaugh & Petrinovich, 1965; McGaugh & Dawson, 1971; and Dawson & McGaugh, 1973). Posttrial injections were suggested (Breen & McGaugh, 1961) as an improvement on the design of earlier studies in which subjects were injected prior to learning trials. Posttrial injections, it was argued, eliminated possible drug effects on sensory, motor and/or motivational processes, thereby making more plausible an interpretation suggesting a drug effect on memory consolidation processes. The posttrial procedure was held to result in subjects who neither learned nor were tested under the direct influence of the drug.

In the first published success at producing performance facilitation with posttrial injections of strychnine sulfate, McGaugh, Thomson, Westbrook and Hudspeth (1962) studied the effect of variations in the training-drug injection interval on the degree of facilitation produced by the drug. Appetitively motivated male and female rats, trained in a Lashley III maze for eight consecutive days, were given intraperitoneal injections of 1.0 mg/kg of strychnine sulfate or saline either 6 minutes before, 1 minute after, 15 minutes after or 90 minutes after each daily

trial. The pretrial and the 1 and 15 minute posttrial, but not the 90 minute posttrial, injections of strychnine sulfate significantly reduced the mean number of errors committed by the rats. The authors concluded that the study provided evidence that strychnine sulfate enhanced performance by facilitating perseverating neural processes that result in the establishment of permanent memories.

A basic assumption in the McGaugh et al. (1962) experiment, as well as in most of the more recent investigations of the facilitative effect of posttrial injections of strychnine sulfate, has been that the typical 24-hour intertrial and retention intervals allow for a reduction of the drug's effect that frees the subject from the direct influence of the drug during subsequent trials. This assumption was challenged by Cooper and Krass (1963) who administered a single intraperitoneal injection of 1.25 mg/kg of strychnine sulfate to female rats either 24 or 72 hours prior to testing on the Hebb-Williams maze problem. Subjects had received two weeks of training in the maze on practice problems of the Hebb-Williams test in order to enable pretest classification of subjects into three areas of adaptation proficiency based on time scores on the practice runs. No training was provided between injection and testing. The single injection facilitated test performance even though administered one or three days prior to the test of its effect. This finding suggests that a 24-hour intertrial or retention interval does not eliminate the possibility that the drug injected posttrial may still be active at the time of test. Therefore, the notion that any facilitation resulting from a posttrial injection must necessarily reflect

the action of the drug on neural correlates of the consolidation process is open to serious question.

Greenough and McGaugh (1965) attempted to evaluate these conflicting explanations of the facilitative effect of posttrial strychnine sulfate injections. McGaugh et al. (1962) had argued that the test performance facilitation obtained with posttrial injections necessitated the conclusion that memory consolidation processes were facilitated. Cooper and Krass (1963) had argued that since the effects of strychnine sulfate injections are still present up to 72 hours after the injection, any test performance facilitation present 24 hours after a posttrial injection may be interpreted as reflecting the effect of the drug on performance factors such as sensory, motor and/or motivational processes during the test itself. In an attempt to obtain unambiguous evidence that posttrial injections of strychnine sulfate facilitate memory consolidation, Greenough and McGaugh (1965) gave rats two training trials followed one week later by five retention trials in a maze identical to that used by McGaugh et al. (1962). Since a one week interval should have allowed for complete metabolism of the drug, any facilitation of retention could not be attributed to facilitation of performance factors resulting from a carryover of the drug effect to test. Intraperitoneal injections of 1.0 mg/kg of strychnine sulfate were given either two days before the training trials (to test for a 48-hour proactive facilitation of learning), immediately after the training trials (to test for facilitation of memory consolidation processes) or two days prior to test (to evaluate 48-hour proactive facilitation of performance factors).

Female rats injected immediately after training performed better than controls and other experimental groups, but the difference reached significance only when just the first three of five test trials were involved in statistical computations. When performance scores on all five test trials were used in statistical computations, there was no statistically significant differences between the groups of female rats. Differences between male rats did not reach significant levels with computations involving all five test trials nor with computations involving only the first three test trials. The failure to find facilitation in male rats and the need for post-hoc elimination of two test trials in order to reveal a significant facilitation in female rats suggests that Greenough and McGaugh (1965) may have committed a Type I error of rejecting a null hypothesis when it is, in fact, correct. Thus, there is reason to doubt Greenough and McGaugh's (1965) conclusion that unambiguous evidence in support of the consolidation interpretation was obtained.

However, there is additional evidence that appears to weigh against the proactive facilitation account of Cooper and Krass (1963) and to support the facilitation of consolidation account offered by McGaugh et al. (1962). McGaugh et al. (1962) and McGaugh and Krivanek (1970) found that the magnitude of the retrograde facilitation produced by posttrial injections of strychnine sulfate was inversely related to the time interval between training and treatment. McGaugh and Krivanek (1970) found that posttrial injections of either .1 or 1.0 mg/kg of strychnine sulfate given to mice were effective in producing facilita-

tion only when given within one hour after training trials, with the greatest amount of facilitation produced by immediately posttrial injections. McGaugh and Dawson (1971) and Dawson and McGaugh (1973) argue that the notion of proactive facilitation cannot explain these findings since the proactive facilitation explanation predicts that later posttrial injections should produce greater facilitation due to the greater temporal proximity to the next day's trials. It is suggested instead that this inverse relationship between length of training-drug injection interval and magnitude of test performance facilitation indicates that later posttrial injections are administered after memory consolidation has been completed. Earlier injections are said to occur at a time when neural correlates of memory consolidation are still susceptible to the positive influence of exogenous agents.

It is possible to suggest yet another account of all the findings of the effects of posttrial injections of strychnine sulfate. This account does not postulate that posttrial injections facilitate memory consolidation processes, but instead explains the phenomenon in terms of Spear's (1971, 1973) attribute-retrieval model of animal memory. In this model, a memory is conceptualized as a collection of attributes representing the events noticed by the organism during memory formation. One or more of these attributes is selected by the experimenter as the target memory. Retention is indicated by performance at test consistent with retrieval of the target memory. Retrieval of the target memory is dependent upon the arousal of an adequate number or kind of the other attributes belonging to the same memory. The arousal of attributes is

said to occur when the animal "notices a cue, external or internal, sufficiently similar to the event represented by that attribute," (Spear, 1973, p. 163). Forgetting occurs when an insufficient number or kind of attributes associated with the target memory are aroused during the testing situation. It follows, then, that the probability of target memory retrieval is a monotonically increasing function of the degree of similarity between the conditions prevalent at training and those at testing.

The attribute-retrieval model can, when combined with assumptions supported by Cooper and Krass' (1963) finding of long term proactive facilitation, explain time-dependent retrograde facilitation. Specifically, if strychnine sulfate is given at a short training-drug injection interval, the physiological consequences of the injection may become an attribute of the memory of the immediately preceding trial. The carryover of the drug effect to the next day's test trials enables these physiological consequences to act as retrieval cues to increase the probability that the target memory associated with the strychnine sulfate injection will be retrieved. The temporal juxtaposition of the training experience and the physiological consequences of the strychnine sulfate injection may result in these consequences becoming a particularly powerful aid to retrieval of the memory of that training experience. Also, since the injection of strychnine sulfate is expected to produce a novel and intensely unusual physiological state in the rat, it can be expected that the physiological consequences may become a particularly salient attribute of the target memory.

Spear's (1971, 1973) model can also provide an explanation of the time-dependent nature of the retrograde facilitation of performance with strychnine sulfate. Injections given at longer training-drug injection intervals occur at a time when the memory of the training experience is no longer susceptible to the influence of exogenous agents. Thus, the physiological consequences of the strychnine sulfate injection do not become an attribute of the memory of the preceding trial. The consequences of the drug carryover to test would then act to hinder retrieval of the target memory because of the differences in conditions prevailing immediately posttrial and at test.

One possible reason why such a retrieval account has not been previously entertained is the common assumption that a drug injection must occur pretrial in order for the drug effect to become an attribute of the memory of that trial (Dawson & McGaugh, 1973). Support for the notion that a posttrial drug injection may become an attribute of the memory of the previous trial is provided by the finding of Chute and Wright (1973) and Wright and Chute (1973) that a posttrial administration of sodium pentobarbitol can result in a state dependent retrieval deficit. In Chute and Wright (1973), fifty naive, male, Sprague-Dawley rats were given one passive avoidance training trial followed within 11 to 13 seconds by either a 12.5 mg/kg injection of sodium pentobarbitol or an equivalent volume of saline. Injections were administered intravenously through a jugular catheter. A retention test was administered 24 hours later, preceded by administration of either sodium pentobarbitol or saline immediately prior to test. Thus, there

were four experimental groups (drug--drug, drug--no drug, no drug--drug and no drug--no drug) and a control group which received neither foot shock during the passive avoidance training nor injections posttrial or pretest. It was found that groups experiencing the same drug immediately posttrial and prior to test (groups drug--drug and no drug--no drug) displayed greater retention as indicated by longer latencies than controls or those experimental subjects experiencing a change in state (groups drug--no drug and no drug--drug). Wright and Chute (1973) replicated the above experiment with minor procedural changes involving intrathoracic rather than intravenous injections and increasing the sodium pentobarbitol dose from 12.5 to 15.0 mg/kg. Again it was found that subjects experiencing the same state immediately after training and at test showed superior performance compared to those subjects experiencing a change in state. To the extent that similar findings would obtain with strychnine sulfate, these findings lend credence to the notion that the physiological consequences of a posttrial injection of strychnine sulfate may become an attribute of the memory of the immediately preceding training experience.

The purpose of the present experiments was to test the account of the effects of posttrial strychnine sulfate injections developed above. The critical test of this hypothesis was conducted in Experiment III. In that experiment all animals were given two massed training trials in a Lashley III maze followed by a retention test seven days later. In the two groups of most concern, all animals received an injection of strychnine sulfate immediately after the final training trial. Prior

to the retention test, half of these subjects received an injection of saline (group D_5-DS; drug within 5 minutes posttrial--different state at test) and the remainder received an injection of strychnine sulfate (group D_5-SS; drug within 5 minutes posttrial--same state at test). To the extent that the physiological consequences of a posttrial strychnine sulfate injection becomes an attribute of the memory of the preceding trial, the physiological consequences of the pretest strychnine sulfate injection should act as retrieval cues, facilitating retrieval of the target memory associated with the training trials. Group D_5-SS subjects should, then, enjoy a presumably powerful addition to the aids to retrieval which all subjects experience as a result of pretest events such as handling and transport to the testing area. Therefore, it is expected that group D_5-SS will be superior to controls given either saline after training and prior to test (group N-SS) or saline after training and strychnine sulfate prior to test (group N-DS). Since the seven day retention interval should allow for metabolism of the posttrial strychnine sulfate injection and complete dissipation of the drug's effect, and since the pretest injection of saline should result in a physiological state different from that prevalent immediately posttrial, it is expected that group D_5-DS will suffer a state dependent retrieval deficit. Therefore, it is expected that group D_5-DS subjects will be inferior in performance at test compared to group N-SS subjects. On the other hand, the facilitation of memory consolidation hypothesis predicts that both groups D_5-SS and D_5-DS will be superior to groups N-SS and N-DS. This is the case since processes of

memory consolidation should be facilitated in both D_5-SS and D_5-DS as a result of the immediately posttrial injections of strychnine sulfate.

The first two experiments were necessary preliminaries to Experiment III. Experiment I was designed to determine the facilitative effect of 1.50 mg/kg of strychnine sulfate in male Sprague-Dawley rats. Experiment II was designed to determine whether strychnine sulfate can act as a discriminative cue in a choice task. The suspected role of strychnine sulfate as a contextual cue aiding retrieval seemed to necessitate an experimental investigation of the rat's ability to differentiate the physiological consequences of a strychnine sulfate injection (a drug state) from the physiological consequences of a saline injection (a non-drug state).

EXPERIMENT I

The present experiment was designed to determine whether 1.50 mg/kg of strychnine sulfate represents a facilitative dose in male Sprague-Dawley rats. A 1.50 mg/kg dose of strychnine sulfate was tested because it is the largest dose found effective in producing facilitation in other studies involving male Sprague-Dawley rats (Gordon, 1977; Gordon & Spear, 1973). Since the influences of drugs on retrieval are most probably dose dependent (Overton, 1974), the desire to use as large a dose of strychnine sulfate as possible in Experiment III necessitates the present test.

Greenough and McGaugh (1965), while obtaining facilitation after a seven day retention interval from an immediately posttrial injection in female rats, failed to obtain the effect with the male Sprague-Dawley

rats used in the experiment. To explain this failure, the authors suggested that the 1.0 mg/kg dose of strychnine sulfate used may have been too high to produce the facilitative effect. The authors referred to two personal communications suggesting that the proper facilitative dose for male Sprague-Dawley rats was between .10 and .20 mg/kg of strychnine sulfate. The successful use of 1.0 and 1.5 mg/kg of strychnine sulfate in other studies of retrograde facilitation (Gordon, 1977; Gordon & Spear, 1973), and the fact that Greenough and McGaugh (1965) required the post-hoc elimination of the last two test trials to obtain a significant facilitation with female rats, provides evidence that Greenough and McGaugh (1965) committed a Type I error. Of course, a negative result in Greenough and McGaugh (1965) for subjects injected immediately posttrial with strychnine sulfate would be expected within the framework of the explanation of retrograde facilitation developed in the introduction since the experimental group of most interest in Greenough and McGaugh (1965) corresponds to group D_5-DS of Experiment III.

Method

Subjects. The subjects were 10 male Sprague-Dawley rats, approximately 90 days old, with previous experience in an operant conditioning experiment. Subjects were maintained at 85% of ad lib. weight, and were individually housed with access to water ad lib.

Apparatus. A Lashley III maze was used for training and testing since the apparatus was used in some previous studies of facilitation with strychnine sulfate (e.g., Greenough & McGaugh, 1965; McGaugh et al.,

1962). Pretraining occured in a straight alley. The alley was 10 cm wide, 23 cm deep and 160 cm long with photoelectric cells at high and low levels at each end of the alley. The start and goal boxes were 10 cm by 23 cm by 20 cm and were each fitted with a guillotine door. A four-unit, 8 cul, Lashley III maze was used for the actual experiment. Each unit was 10 cm by 13 cm by 120 cm. Doorways in the alleys were 30 cm from the ends of the culs. The floor was marked with narrow white lines 5 cm from both sides of each doorway. The start and goal boxes were each 10 cm by 13 cm by 30 cm. The doorways of the start and goal boxes were fitted with guillotine doors. Both apparatus were painted grey and were covered by wire mesh. The alley and the Lashley III maze are depicted in Figures 1 and 2, respectively.

Procedure. Subjects were first pretrained to run a straight alley for a reinforcer consisting of four 45 mg food pellets. Five spaced trials were run daily for seven days. Only those rats achieving an average daily running speed of 45 seconds or less by the seventh day were included in the remainder of the experiment. All 10 subjects satisfied this criterion and, therefore, participated throughout the remainder of the experiment. No training was given on Day 8, and 48 hours after the last session of preliminary training the subjects received two massed learning trials in the Lashley III maze with food pellet reward at the completion of each trial. An error was recorded each time a rat's head crossed a white line two inches past the choice point in a blind alley. Retracing in the alleys was not considered an error. After the learning trials, subjects were randomly assigned to one of two groups and received

immediate posttrial injections of 1.50 mg/kg of strychnine sulfate or 1.50 mg/kg of saline. Twenty-four hours after the learning trials, each subject received five massed test trials in the Lashley III maze with food pellet reward. Errors were recorded in a manner identical to that used during learning trials in the Lashley III maze.

Results.

The results are presented in Table 1 in terms of the mean number of errors on the two training trials and the five retention trials. The two groups did not differ in terms of the number of errors committed on the final training trial ($t < 1$), indicating that differences in retention were not confounded by differences in degree of learning. Fewer errors were committed on the first test trial by subjects injected with strychnine sulfate than by those injected with saline. Moreover, the worst performer in the strychnine sulfate treated group committed fewer errors than even the best performer in the saline treated group. The difference in first trial errors between the two groups was found to be statistically significant (t (8) = 4.13, $p < .01$, one-tailed). Examination of all five retention test trials revealed that subjects injected posttrial with strychnine sulfate performed better over trials than subjects injected with saline. There was a general tendency for subjects to commit fewer errors across test trials (that is, relearning was evidenced) and the rate of relearning did not differ between the two groups. An analysis of variance performed on all five test trials revealed a significant effect of groups (F (1,8) = 32.95, $p < .01$), a significant effect of trials (F (4,32) = 2.76, $p < .05$) and a nonsignificant

difference between the slopes of the relearning curves of the two groups (F (4,32) = 1.78, $p > .05$).

Discussion.

The results clearly indicate that 1.50 mg/kg is a facilitative dose of strychnine sulfate for male Sprague-Dawley rats used in this task. This reinforces the notion that the failure to obtain facilitation of retention in male Sprague-Dawley rats in Greenough and McGaugh (1965) was not due to the 1.0 mg/kg dose of strychnine sulfate being too high to exert a facilitative effect. The failure to obtain facilitation was more probably due to the fact that the seven day retention interval allowed for a complete metabolism of the strychnine sulfate and a total dissipation of its effects. Since subjects in Greenough and McGaugh (1965) were under the influence of the drug immediately posttrial, but were not under the influence of the drug at test, there were no cues associated with the physiological consequences of strychnine sulfate to aid retrieval.

It should be noted that because a 24-hour retention interval was used in the present experiment, the facilitation of retention resulting from the posttrial injections of strychnine sulfate could be explained in terms of either memory consolidation or retrieval processes. The lack of difference between groups in the slopes of the relearning curves suggests that an incremental facilitation of sensory, motor and/or motivational processes did not occur. Such a facilitation of performance factors would most probably have resulted in a steeper drop in errors over the five retention trials for the group under the influence of the

strychnine sulfate carryover at test. However, it is possible that a facilitation of performance factors may have occured on the first test trial and maintained the same level across the remaining test trials. Such an effect would summate with facilitation of memory consolidation or with a facilitation of retrieval. The notion of a single level of facilitation of performance factors maintained across trials is consistent with the lack of difference in the slopes of the relearning curves of the two groups.

EXPERIMENT II

The purpose of this experiment was to determine whether strychnine sulfate can act as a discriminative cue in a choice task. The retrieval hypothesis of facilitation of retention suggests that the physiological consequences of the posttrial strychnine sulfate injection carry over to test and act to aid retrieval. Since Spear's (1971, 1973) model holds that attributes of a memory consist of those events to which the animal attends, it seemed essential to test whether the rat can attend to, and base a discriminative choice on, a strychnine sulfate injection.

Method.

Subjects. The subjects were 10 naive, male Sprague-Dawley rats maintained at 85% of ad lib. weight, individually housed with access to water ad lib. All subjects were approximately 90 days old at the start of discrimination training.

Apparatus. The apparatus was a standard T-maze. The T-maze consisted of a start box and alley with an arm at a right angle on each side of the alley's end. The start box was 10 cm by 13 cm by 26 cm and was

fitted with a guillotine door. The alley was 10 cm by 13 cm by 48 cm with guillotine doors at the choice points which led to the arms. Each arm was 10 cm by 13 cm by 48.5 cm and was equipped with a 9.5 cm by 13 cm by 12 cm goal box. The goal boxes were placed at a right angle to the arms of the maze so that the contents could not be seen by subjects at the choice point. The T-maze used in the experiment is depicted in Figure 3.

Procedure. Subjects received three daily familiarization sessions of five minutes each. Food pellets were scattered throughout all parts of the T-maze and subjects were allowed unimpeded exploration of the maze during the sessions. Following familiarization sessions, the subjects began receiving drug discrimination learning trials every other day. A dose of 1.50 mg/kg of strychnine sulfate or 1.50 mg/kg of saline was injected intraperitoneally 15 minutes prior to the learning trials. Initially, the two groups of subjects were run on alternate days (a 48-hour intertrial interval) to allow for metabolism of the drug to less significant levels. Casual observation suggested that concern for drug carryover was unfounded, and therefore, after all subjects had received three learning trials under each drug state, the experimental procedure was modified to allow daily learning sessions. The contents of the pretrial injections were determined in a quasi-random fashion to insure discrimination on the basis of drug state rather than a session to session alternation of response. Group A subjects were required to turn right in the strychnine sulfate condition and left in the saline condition. Group B subjects were required to turn left in the strychnine sulfate condition

and right in the saline condition. Sessions consisted of 10 appetitively motivated (food pellet reward) massed trials with unlimited corrections. Subjects received 18 days of learning sessions in three blocks of six days each. Performance on the first trial was recorded as a measure of the discriminability of the strychnine sulfate condition versus the saline condition. Subjects were said to have learned the discrimination when it was clear that the response on the first trial of each session was under control of the presession injection rather than the previous day's contingencies.

Results and Discussion.

Performance on the first trial of each daily session is expressed in Figure 4 as a function of the drug state induced prior to the session. Initially, first trial performance was more dependent on the contingencies prevalent during the subject's most recent session than on the contingencies relevant to the subject's drug state. Performance on the first trial gradually came under the control of the presession drug injection until, finally, first trial responses were under complete control of the presession injections rather than under the control of the contingencies relevant to the previous day's training. This experiment clearly demonstrates that rats can discriminate between the physiological consequences of a strychnine sulfate injection and the physiological consequences of a saline injection. This fact suggests that the physiological consequences of strychnine sulfate may, indeed, act as contextual cues in the common retrograde facilitation paradigm utilizing a 24-hour retention interval.

EXPERIMENT III

This experiment was primarily a test between the account of time-dependent retrograde facilitation based on Spear's (1971, 1973) attribute-retrieval model of animal memory and the account of the phenomenon based on the facilitation of memory consolidation hypothesis. The experiment was similar to Greenough and McGaugh (1965) in that the same apparatus was used and a seven day retention interval was employed. The seven day retention interval was designed to insure that no carry-over of the physiological consequences of the posttraining injections occured. To enable a comparison of the two explanations of retrograde facilitation, half of the subjects from each posttraining treatment group were injected with strychnine sulfate prior to test while the remaining half received an equivalent injection of saline. The retrieval hypothesis predicts that, among subjects injected immediately posttrial with strychnine sulfate, only those reinjected with strychnine sulfate prior to test will reveal a facilitation of retention. Moreover, the retrieval hypothesis predicts that, within each posttraining treatment group, those subjects experiencing the same state posttraining and at test will perform better than those experiencing a change in state. The memory consolidation hypothesis, on the other hand, predicts that all subjects injected with strychnine sulfate immediately posttrial will show facilitation of retention regardless of the nature of the pretest injection. Moreover, the memory consolidation hypothesis makes no predictions of differences within posttraining groups dependent on the similarity of conditions prevalent posttraining and at test.

Method

Subjects. The subjects were 65 naive, male Sprague-Dawley rats, approximately 90 days old. Subjects were maintained at 85% of ad lib. weight, were individually housed, and had access to water ad lib.

Apparatus. The straight alley and Lashley III maze used in Experiment I were again employed.

Procedure. Subjects were first pretrained to run a straight alley for food pellet reinforcement. Five spaced trials were run daily for seven days. Only those rats achieving an average daily running speed of 45 seconds or less by the seventh day were included in the remainder of the experiment. Only one subject failed to meet this criterion and that subject was, therefore, dropped from the remainder of the experiment. Following the preliminary training (on the eigth day) subjects received two massed learning trials in the Lashley III maze with food pellet reward at the trials' end. An error was recorded each time a rat's head crossed a white line two inches past the choice point in a blind alley. Prior to the learning trials, subjects were randomly assigned to six groups; D_5-DS in which subjects were given strychnine sulfate immediately posttrial and saline 15 minutes prior to test, D_5-SS in which strychnine sulfate was given immediately posttrial and again prior to test, D_{120}-SS in which strychnine sulfate was given 120 minutes posttrial and saline prior to test, D_{120}-DS in which strychnine sulfate was given 120 minutes posttrial and again prior to test, N-SS in which saline was given immediately posttrial and prior to test, and N-DS in which saline was given immediately posttrial and strychnine sulfate

prior to test. All injections consisted of 1.50 mg/kg of strychnine sulfate or saline and were administered intraperitoneally. A seven day retention interval intervened between training and testing. Testing consisted of five massed trials in the Lashley III maze with food pellet reward. Errors were recorded in a manner identical to that used during the learning trials in the Lashley III maze.

Results.

The results are presented in Table 2 in terms of the mean number of errors on the two training trials and the five retention trials. The groups did not differ in terms of the mean number of errors committed on the final training trial (F (5,58) = 1.47, $p > .05$), indicating that differences in retention were not confounded by differences in degree of learning. Examination of errors on the first retention trial shows that group D_5-SS demonstrated enhanced retention while group D_5-DS demonstrated a retrieval deficit. A Neuman-Keul's test revealed that group D_5-SS committed significantly fewer errors than any other group ($p < .01$), and that no further comparisons were significant. A significant posttraining treatment effect was obtained (F (2,58) = 4.29, $p < .05$). The results of the Neuman-Keul's test suggest that the significant posttraining treatment effect resulted from the superior performance of group D_5-SS. Groups experiencing the same state immediately posttrial and at test demonstrated significantly superior first trial retention when compared to groups experiencing a change in state (F (1,58) = 23.69, $p < .001$). The corresponding means for the same state and different state groups were 3.42 and 4.68, respectively. The difference between the same state

and different state groups was larger within the D_5 posttraining group than within the D_{120} and N posttraining groups, as indicated by a significant posttraining treatment X state similarity interaction (F (2,58) = 3.55, $p < .05$). Finally, groups experiencing the drug pretest (groups D_5-SS, D_{120}-DS and N-DS) made only slightly fewer errors than those experiencing saline pretest (groups D_5-DS, D_{120}-SS and N-SS), $\bar{X}$ = 3.98 and 4.12, respectively. Since D_{120}-DS and N-DS committed more errors than D_{120}-SS and N-SS, respectively, the apparent facilitation of performance by the pretest injection of strychnine sulfate was due solely to the superior performance of group D_5-SS compared to D_5-DS.

Examination of the error data for all five test trials reveals a pattern of findings similar to those found using only the first retention test trial. A Neuman-Keul's test again revealed that group D_5-SS committed significantly fewer errors than any other group ($p < .01$), and that no further comparisons were significant. Groups tested under the same state as that prevalent immediately posttrial performed significantly better than groups experiencing a change in state (F (1,58) = 25.10, $p < .001$). The corresponding means for the same state versus different state groups were 2.41 and 3.85, respectively. The posttraining treatment X state similarity interaction was again significant (F (2,58) = 3.58, $p < .05$), due to the greater difference between the same state and different state conditions within the D_5 posttraining treatment group than within the D_{120} and N posttraining treatment groups. Finally, groups injected pretest with strychnine sulfate committed only slightly fewer errors than those injected pretest with saline, $\bar{X}$ = 3.09 and 3.17,

respectively. This difference was again entirely due to the superior performance of group D_5-SS over group D_5-DS rather than a facilitation of performance factors in all subjects given strychnine sulfate prior to test. Examination of the error data for all five test trials also revealed that there was a general tendency for all groups to commit fewer errors across trials (that is, relearning was evidenced). A significant effect of trials was found (F (4,240) = 65.61, $p < .001$), but trials did not interact with any treatment factor or combination of treatment factors.

Discussion.

These results clearly support the attribute-retrieval interpretation of time-dependent retrograde facilitation of retention by strychnine sulfate. Moreover, the data provide no support for the notion that posttrial administration of strychnine sulfate enhances processes of memory consolidation or that performance factors such as sensory, motor and/or motivational processes are facilitated at test. Subjects receiving an injection of strychnine sulfate immediately posttrial demonstrated enhanced retention only when the contextual cues of the physiological consequences of strychnine sulfate were reinstated prior to test, thus providing an additional powerful aid to retrieval of the target memory. Further support for the attribute-retrieval model was provided by the finding that groups experiencing no change of state from immediately posttrial to test committed fewer errors than groups experiencing a change in state. The fact that group D_{120}-DS performed more poorly than group D_{120}-SS suggests that the 120 minute posttrial injection

occured too late for the physiological consequences of the strychnine sulfate injection to have become an attribute of the memory of the preceding training.

General Discussion

The results of these experiments provided no support for the memory consolidation hypothesis of time-dependent retrograde facilitation of retention nor did they support an explanation in terms of facilitation of performance factors such as sensory, motor and/or motivational processes. As predicted, the experiments were consistent with assumptions based on the finding of long term proactive facilitation by strychnine sulfate (Cooper & Krass, 1963) and the assumptions of Spear's (1971, 1973) attribute-retrieval model of animal memory.

The results of these experiments make it possible to provide an alternate explanation for all studies demonstrating retrograde facilitation of retention which were previously thought to be explicable only in terms of facilitation of memory consolidation processes. In McGaugh et al. (1962) and McGaugh and Krivanek (1970), rats and mice, respectively, were given posttrial injections of strychnine sulfate or saline at various training-drug injection intervals. When tested 24 hours later, subjects injected with strychnine sulfate posttrial revealed greater retention. Furthermore, the degree of facilitation was inversely related to the length of the training-drug injection interval and little or no facilitation occured with a training-drug injection interval greater than one hour. These results were interpreted by the authors as evidence that the posttrial strychnine sulfate injection had facilitated memory

consolidation processes. Failure to obtain facilitation at greater than one hour training-drug injection intervals was, the authors claimed, due to the fact that the injections occured at a time when the neural correlates of memory consolidation were completed, thus eliminating the susceptibility of the memory to the positive influence of exogenous agents. Dawson and McGaugh (1973) have emphatically denied that an interpretation such as that advanced in the introduction of the present paper could explain the results of McGaugh et al. (1962) and McGaugh and Krivanek (1970) since "the drug is not present in the animal either at the time of training or at the time of retesting," (Dawson & McGaugh, 1973, p. 83).

The assumption that subjects in McGaugh et al. (1962) and McGaugh and Krivanek (1970) were not under the influence of the drug during the retention test given 24 hours posttraining is not supported by Cooper and Krass (1963) who found that strychnine sulfate could exert a positive proactive effect on performance up to 72 hours after a single injection. Moreover, the present experiments provide evidence that a posttrial injection of strychnine sulfate can become an attribute of the memory of the preceding trial, even though the animal is not under the influence of the drug during training. Thus, the facilitation at short training-drug injections found in McGaugh et al. (1962) and McGaugh and Krivanek (1970) can be explained from the fact that the physiological consequences of the posttrial strychnine sulfate injection became an attribute of the memory of the previous trial and from the fact that the physiological consequences of the drug carryover across the 24 hour retention interval acted as a retrieval cue to alleviate the retention decrement found in

controls due to the passage of time. This interpretation is supported by the results of Experiment III in which the immediate posttrial injection of strychnine sulfate was effective in producing a facilitation of retention only when the physiological consequences of strychnine sulfate were reinstated prior to the test given after a seven day retention interval (that is, group D_5-SS subjects were superior to controls and group D_5-DS subjects). The failure to obtain a facilitation of retention in subjects who did not have the physiological consequences of strychnine sulfate reinstated prior to the test (group D_5-DS) suggests strongly that the facilitation of retention found in McGaugh et al. (1962) and McGaugh and Krivanek (1970) was a result of the facilitation of processes of retrieval rather than a result of facilitation of memory consolidation processes.

The results of Experiment III also enable an alternate explanation of the time-dependent nature of the retrograde facilitation phenomenon. The superior performance of subjects experiencing the same state posttrial and at test compared to those experiencing a change in state suggests that the injection given at a longer training-drug injection interval occurs too late for the physiological consequences of strychnine sulfate to become an attribute of the memory of the preceding trial rather than occuring too late to facilitate the perseverative neural processes of memory consolidation.

The above explanation of facilitation of retention in terms of Spear's (1971, 1973) attribute-retrieval model can also be used to explain the facilitation of performance found with multiple injections of

strychnine sulfate (Hudspeth, 1964; Krivanek & Hunt, 1967; Ross, 1964). In each of these experiments, subjects experiencing daily posttrial injections of strychnine sulfate performed significantly better across trials than controls given saline posttrial. While the authors attributed the results to a facilitation of memory consolidation processes, it is possible to explain the results in terms of facilitation of retrieval. Each day's posttrial injection of strychnine sulfate became an attribute of the memory of the preceding trial. Due to the 24-hour intertrial interval employed in these multiple injection studies, the physiological consequences of the posttrial strychnine sulfate injections carried over to the next day's trials and acted as aids to retrieval. Because injections of strychnine sulfate occured after every daily session, strychnine sulfate treated subjects enjoyed enhanced retrieval during all sessions following the first posttrial injection.

Finally, there remains the finding of the facilitation of reactivated memories, a phenomenon explicable by Spear's model but difficult to reconcile with the facilitation of memory consolidation hypothesis. Gordon and Spear (1973, Experiment 2) trained half of 80 male Sprague-Dawley rats in a passive avoidance (PA) task to a criterion of five consecutive avoidances within eight trials. The remaining 40 subjects were controls who experienced the same amount of time as experimental subjects in the holding cages and the training apparatus. These controls did not experience footshock and were allowed unimpeded exploration of the training apparatus. Seventy-two hours after training, most of the subjects were placed in the training apparatus for 60 seconds while the CS

used in PA training was on. This treatment is one which had been demonstrated to be effective in reactivating the memory of previous training or experience in an apparatus (Spear, 1973). Immediately after the reactivation treatment, subjects were injected with either 1.50 mg/kg of strychnine sulfate or saline. Eight of the subjects who had received PA training did not undergo the reactivation treatment but did receive an equivalent injection of strychnine sulfate 72 hours after PA training. All subjects were tested on an active avoidance (AA) task 24 hours after the injections. The authors expected that the PA training would result in negative transfer to the AA test, since the response required on the AA test was diametrically opposed to that required during PA training. Therefore, any facilitation of the memory of the PA training would result in greater negative transfer indicated by decrements in performance on the AA test. Since the period of memory consolidation is generally defined as occuring within one hour posttrial (Dawson & McGaugh, 1973), any facilitation of retention of subjects given the strychnine sulfate injection 72 hours posttraining (that is, following the reactivation treatment) would argue against a strict memory consolidation hypothesis of facilitation of retention by posttrial strychnine sulfate injections.

As expected, subjects given strychnine sulfate after the reactivation treatment performed significantly worse on the AA test than all other groups, thus indicating that the 72 hour posttrial injection facilitated retention of the PA training. This result is inconsistent with the memory consolidation hypothesis, which predicted that the 72 hour posttrial injection would be unable to facilitate retention of the PA

training. While a supporter of the memory consolidation hypothesis could suggest that the reactivation treatment reinitiated the process of memory consolidation, this would constitute an unacceptable change in the way consolidation has been previously defined by such researchers as Dawson and McGaugh (1973). Gordon and Spear (1973) note the facilitation of retention produced by the 72 hour posttrial injection of strychnine sulfate suggested that the usual failure to facilitate retention with an injection given at a greater than one hour training-drug injection interval (McGaugh et al., 1962; McGaugh & Krivanek, 1970) could not be due solely to the fact that the memory of the preceding trial had already been consolidated.

Lewis (1969) has noted that a memory can often be disrupted whenever it is going from a stored to active state, or vice versa. Gordon and Spear (1973) suggested that a memory may be susceptible to facilitation at such times also. Spear's (1971, 1973) model provides a means of explaining how facilitation of a reactivated memory (a memory presumably going from a stored to active state) could occur. If it is assumed that the reactivation of a memory results in a susceptibility to additional influences during the time the memory is re-active, then it is likely that the postreactivation strychnine sulfate injection resulted in the physiological consequences of strychnine sulfate becoming an attribute of the reactivated memory. The 24 hour retention interval of Gordon and Spear (1973, Experiment 2) enabled the carryover of the physiological consequences of strychnine sulfate to act as retrieval cues to facilitate the memory of the PA training and depress performance on the AA test.

In a further study of the effects of postreactivation injections of strychnine sulfate (Gordon, 1977, Experiment 1) investigated the time-dependent nature of the phenomenon. The design of Gordon (1977, Experiment 1) conformed closely to that of Gordon and Spear (1977, Experiment 2) except that subjects were given injections of strychnine sulfate or saline at .25, 2, 5, 15 or 30 minutes after the reactivation treatment. Only subjects injected at .25 and 2 minutes after the 72 hour postreactivation treatment performed significantly more poorly on the AA test than controls, showing that facilitation of retention resulting from a postreactivation injection of strychnine sulfate was a time-dependent phenomenon. While the results of Gordon (1977, Experiment 1) cannot be explained in terms of the memory consolidation hypothesis any more easily than can the results of Gordon and Spear (1973, Experiment 2), the use of a 24 hour retention interval suggests that Spear's model can again explain the facilitation of retention. The time-dependent nature of the facilitation can be dealt with by suggesting that injections given at 5 or more minutes posttrial occur too late to enable the physiological consequences of the strychnine sulfate injection to become an attribute of the memory of the PA training. Further research is required to explain the different facilitation gradients for newly consolidating and reactivated memories (Gordon, 1977, Experiments 1 and 2).

In conclusion, the results of the present experiments provide an alternate explanation in terms of Spear's (1971, 1973) attribute-retrieval model of animal memory and long term drug carryover effects

(Cooper & Krass, 1963) for all studies of time-dependent retrograde facilitation with strychnine sulfate previously thought to be explicable only in terms of the memory consolidation hypothesis expressed by Dawson and McGaugh (1973). In addition, Spear's model can account for facilitation of reactivated memories, a phenomenon not easily explained by the memory consolidation hypothesis. Therefore, while the possibility that posttrial injections of strychnine sulfate may facilitate memory consolidation processes cannot be entirely ruled out, it must be allowed that there has not yet been a study which has unambiguously demonstrated that retrograde facilitation with strychnine sulfate is the result of facilitation of memory consolidation processes rather than a result of drug carryover and a facilitation of retrieval.

References

Breen, Richard A., & McGaugh, James L. Facilitation of maze learning with posttrial injections of picrotoxin. Journal of Comparative and Physiological Psychology, 1961, 34(5), 498-501.

Chute, D. L., & Wright, D. C. Retrograde state dependent learning. Science, 1973, 180, 878-880.

Cooper, R. M., & Krass, M. Strychnine: Duration of the effects on maze-learning. Psychopharmacologia, 1963, 4, 472-475.

Dawson, R. G., & McGaugh, J. L. Drug facilitation of learning and memory. In J. Anthony Deutsch (Ed.), The Physiological Basis of Memory. New York: Academic Press, 1973.

Gordon, W. C. Susceptibility of a reactivated memory to the effects of strychnine: A time-dependent phenomenon. Physiology and Behavior, 1977, 18, 95-99.

Gordon, W. C., & Spear, N. E. The effects of strychnine on recently acquired and reactivated passive avoidance memories. Physiology and Behavior, 1973, 10, 1071-1075.

Greenough, W. T. & McGaugh, J. L. The effect of strychnine sulfate on learning as a function of time of administration. Psychopharmacologia, 1965, 8, 290-294.

Hudspeth, W. J. Strychnine: Its facilitating effect on the solution of a simple oddity problem by the rat. Science, 1964, 145, 1331-1333.

Krivanek, J. A., & Hunt, E. The effect of posttrial injections of pentylenetetrazole, strychnine and mephenesin on discrimination learning. Psychopharmacologia, 1967, 10, 189-195.

Lashley, K. S. The effects of strychnine and caffeine upon the rate of learning. Psychobiology, 1917, 1, 141-170.

Lewis, D. J. Sources of experimental amnesia. Psychological Review, 1969, 76, 461-472.

McGaugh, J. L., & Dawson, R. G. Modification of memory storage processes. In W. K. Honig and P. H. R. James (Eds.). Animal Memory. New York: Academic Press, 1971.

McGaugh J. L., & Krivanek, J. A. Strychnine effects on discrimination learning in mice: Effects of dose and time of administration. Physiology and Behavior, 1970, 5, 1437-1442.

McGaugh, J. L.; & Petrinovich, L. F. Effects of drugs on learning and memory. International Review of Neurobiology, 1965, 8, 139-196.

McGaugh, J. L., & Thomson, C. W. Facilitation of simultaneous discrimination learning with strychnine sulphate. Psychopharmacologia, 1962, 3, 166-172.

McGaugh, J. L., Thomson, C. W., Westbrook, W. H., & Hudspeth, W. J. A further study of learning facilitation with strychnine sulfate. Psychopharmacologia, 1962, 3, 352-360.

Overton, D. A. Experimental methods for the study of state-dependent learning. Federation Proceedings, 1974, 33, 1800-1813.

Petrinovich, L. F. Facilitation of successive discrimination learning by strychnine sulfate. Psychopharmacologia, 1963, 4, 103-113.

Petrinovich, L. F. Drug facilitation of learning: Strain differences. Psychopharmacologia, 1967, 10, 375-378.

Ross, R. B. Effects of strychnine sulphate on maze learning in rats.

Nature, 1964, 201, 109-110.

Spear, N. E. Forgetting as retrieval failure. In W. K. Honig and P. H. R. James (Eds.), Animal Memory. New York: Academic Press, 1971.

Spear, N. E. Retrieval of memory in animals. Psychological Review, 1973, 80, 163-194.

Wright, C. I., & Chute, D. L. State Depdnent learning produced by post-trial intrathoracic administration of sodium pentobarbitol. Psychopharmacologia, 1973, 31, 91-94.

Table 1

Mean Number of Errors

Experiment I

	Training		Testing					
	1	2	1	2	3	4	5	n
Saline-treated	6.4	6.0	4.6	3.0	3.2	2.8	2.2	5
Strychnine sulfate-treated	6.2	5.8	1.0	1.2	1.0	1.4	0.4	5

Table 2

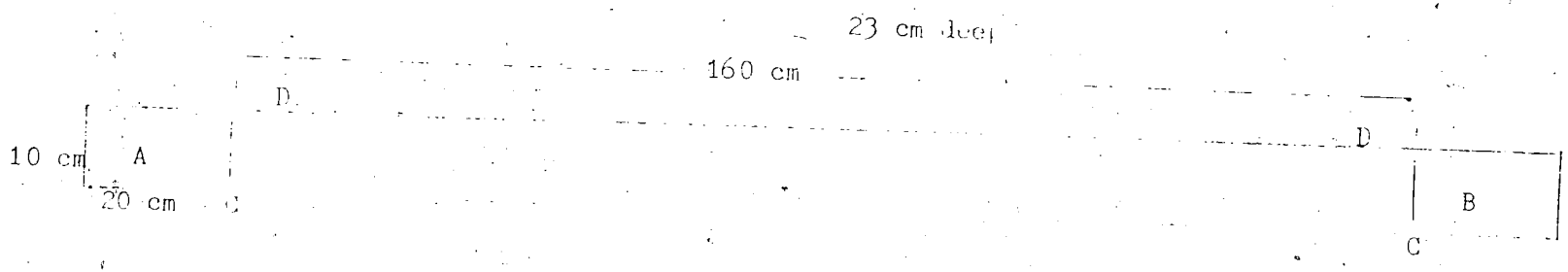
Mean Number of Errors

Experiment III

Group	Training 1	Training 2	Testing 1	Testing 2	Testing 3	Testing 4	Testing 5	Post $\bar{X}$	n
L_0-SS	5.27	5.09	2.45	1.91	1.45	0.82	0.64	1.45	11
L_{120}-SS	5.45	4.00	3.82	3.54	2.91	2.54	1.73	2.91	11
N-SS	5.09	4.54	4.00	3.45	2.73	2.18	2.00	2.87	11
D_0-SS	5.45	4.45	4.54	4.18	3.91	3.09	3.00	3.74	11
D_{120}-SS	5.30	4.30	4.70	4.70	4.30	3.70	3.30	4.14	10
N-LS	4.80	3.80	4.80	3.70	3.40	3.40	3.10	3.68	10

Figure 1

Straight Alley



Scale: 1 cm = 10 cm

A = Start box
B = Goal box
C = Guillotine doors
D = Photoelectric cells

Figure 2

Lashley III maze

Figure 3
Standard T-maze
Scale: 1 cm = 10 cm
A = Start box
B = Goal box
C = Guillotine doors
10 cm
26 cm
A
C
13 cm deep
40 cm
9.5 cm
B
9.5 cm
48.5 cm
C
C
48.5 cm
10 cm

Figure 4

Experiment III