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**THOMPSON, Venan Edward, 1934-
NEONATAL ORBITOFRONTAL LOBECTOMIES AND
DELAYED-RESPONSE BEHAVIOR IN CATS.**

**The Ohio State University, Ph.D., 1965
Psychology, experimental**

University Microfilms, Inc., Ann Arbor, Michigan

NEONATAL ORBITOFRONTAL LOBECTOMIES

AND

DELAYED-RESPONSE BEHAVIOR IN CATS

DISSERTATION

Presented in Partial Fulfillment of the Requirements for the
Degree Doctor of Philosophy in the Graduate School of
The Ohio State University

By

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* * * * *

The Ohio State University
1965

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ACKNOWLEDGMENTS

Most sincere thanks are due Dr. D.R. Meyer who has served as Mentor, Adviser, and under whose direction this research was conducted.

Dr. R. Miles and Dr. W. Howell, the other members of the Reading Committee, have served with utmost patience. For their kind and ready assistance in the many moments of need, I am most grateful and appreciative.

Many members of the Laboratory of Comparative and Physiological Psychology contributed their help. Dr. P.M. Meyer perfected and trained the author in the surgical techniques which we used. Lewis Bettinger and Mildred Huss assisted in collecting the data. Allan Wetzel was always available to spend many hours in surgery. Roy Anderson, Jay Braun, Thomas LeVere, and David Yutzey all assisted in surgery and in many small ways to numerous to mention.

Thanks are also due Dr. P.C. Bucy whose histology laboratory prepared many of the slides for the histopathological reconstruction of the brains of the operated animals, and whose assistant prepared the Figure.

This research was supported in part by Grants No. MH-2035 and MH-2611 from the National Institutes of Health to the Laboratory of Comparative and Physiological Psychology.

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CHAPTER I

HISTORICAL REVIEW

Frontal lobe function and delayed-response behavior

The present paper deals with two related topics. The first is the effect of frontal lobectomy on the acquisition of delayed-response behavior in cats. Secondly we are concerned with age at the time of frontal lobectomy as a factor in the learning of delayed responses.

Frontally lobectomized cats do not retain a preoperatively learned capacity to solve indirect, three-choice, delayed-response problems (Lawicka & Konorski, 1961). During relearning sessions the error and response pattern of the animals change. Prior to surgery the animals make predominately anti-perseverative errors and are able to respond correctly, irrespective of bodily orientation, at the end of the delay period. After surgery the animals make predominately perseverative and preference-omission errors and, in addition, are very sensitive to bodily orientation cues.

In most delayed-response experiments the animal is asked to choose between two responses, and noncorrection procedures are typically employed. Lawicka & Konorski gave their animals three choices and, in addition, permitted correctional responses which were never reinforced. Their cats, after surgery, made significantly more correct correctional responses than erroneous ones. On the basis of these results, the authors suggested that the error tendencies produced by frontal lobectomy prevented the exhibition of some retention of delayed responding.

In their opinion, the effect of the retention testing sessions was essentially a training of the cats to overcome these interferences.

The relevance of these results to the results of other experiments in the area of frontal lobe lesions and delayed-response learning becomes apparent when viewed in historical perspective. Jacobsen (1935) reported that monkeys with frontal lobectomies are unable to solve a direct form of delayed-response problem. Finan (1942) replicated this experiment, but on some trials forced his monkeys to make the correct response and obtain a reward. On the choice trials which followed the forced trial, the animals responded correctly; but on those trials which were not preceded by forced trials, the animals responded at chance levels. Of the number of interpretation available to explain this result, the one most parsimonious with the Lawicka & Konorski experiment is that on the trial after the forced trial, the animals were making perseverative responses. In the Lawicka & Konorski experiment, these responses were classified as errors, whereas in Finan's experiment, they were the correct responses.

Another manner of considering these experiments is to say that the animals exhibited "response perseverative" behaviors. These are responses in which the same motor acts occur on successive trials. The complementary class of behaviors are those which can be called "stimulus perseverative" behaviors. This type of behavior is defined by perseverative responses to a class of stimuli and do not necessarily include the same motor act. This type of behavior was first noted in frontally lesioned monkeys by Settlage, Zable, & Harlow (1948), and has been investigated more recently by Brush, Mishkin, & Rosvold (1961). When

Lawicka & Konorski's cats made preference-omission errors, they were exhibiting "stimulus perseverative" behaviors.

Stanley & Jaynes (1949) proposed the "act inhibition" theory which suggested that the frontally lesioned preparation was incapable of inhibiting its predominant response tendencies. Lawicka & Konorski believe that this theory also accounts for the behavior of their cats. This implies that they consider the two classes of behavior (response perseverative responses and stimulus perseverative responses) as equivalent. But since theirs was the first experiment in which these two classes were clearly differentiated from each other, this is an assumption which may not be valid and awaits empirical assessment.

Our primary interest in the Lawicka & Konorski experiment arose when we were searching for a delayed-response method of assessing the factor of age at the time of surgery on the recovery from frontal lobectomy in cats. Their procedure, which permits one to examine several types of error, seemed to us to be a suitable behavioristic framework for the kind of study which we had in mind.

Recovery of function

Many behaviors which are markedly impaired by neural extirpation in adulthood apparently are much less affected by a comparable lesion which is produced perinatally. In one of the earliest experiments concerned with age as a factor in recovery, Kennard (1936; 1938; 1940; 1942) examined motor behavior of monkeys with extensive lesions of the motor and premotor cortex. She found that the monkeys which received the lesions prior to one year of age were minimally impaired on the neurological tests for the effects of the operation. In some of the

subjects the neurological symptoms disappeared within a week. In contrast, the monkeys lesioned as adults exhibit permanent motor deficits when neurologically examined repeatedly during a period of months.

Doty (1953) tested cats which had received lesions of the visual cortex as neonates. He reported that when tested in adulthood these cats were able to learn a pattern discrimination, but were impaired on subtle problems which involve a visual presentation. When tested at maturity on a tactile discrimination problem, cats which sustained lesions of the somatic cortex when six days old (1) can discriminate between a rough and smooth surface; but (2) cannot discriminate between two degrees of roughness (Benjamin & Thompson, 1959). Cats similarly prepared as adults cannot make the first discrimination, while normal Ss can make both.

More complete recovery has been obtained when, neonatally, the cortical areas mediating audition were removed. Sharlock, Tucker, & Strominger (1963) observed that these adult cats solved an auditory pattern discrimination problem at levels comparable with those of normal cats, even though adult-lesioned cats were quite severely impaired.

Less is known about the consequences of the age effects of brain damage if associative cortex is removed in infancy and more complex behaviors investigated. Monkeys with neonatal lobectomies of the frontal area can solve the delayed-response problem (Akert, Orth, Harlow, & Schiltz, 1960), while the adult-lobectomized typically cannot (Jacobsen, 1935).

CHAPTER II

INTRODUCTION

Several lines of evidence suggest that the effects of early lesions of the neocortex differ rather markedly from the effects produced by comparable ablation in adulthood. For example, almost complete recovery of function is noted after perinatal lesions of sensory cortex in the cat (Benjamin & Thompson, 1959; Doty, 1953; Sharlock, Tucker, & Strominger, 1963). In the monkey sparing has been noted after early lesions of the sensorimotor cortex (Kennard, 1936; 1938; 1940; 1942), and the perinatal frontal animal performs delayed responses at a normal level (Akert, Orth, Harlow, & Schiltz, 1960).

The present studies were concerned with the effects of age at the time of orbitofrontal extirpation upon the delayed-response performances of cats and kittens in a three-choice situation. We have used this situation so that, in addition to the usual measures of performance, measures of the changing probabilities of different kinds of errors also could be taken. The approach is patterned after some of the procedures followed by Lawicka & Konorski (1961), but our apparatus differs from their test arrangement in a few significant respects.

METHOD

Subjects

Experiment I. Sixteen naive adult cats were assigned to either an adult-operated group (AO; $N = 9$), or to an unoperated control group (AN; $N = 7$).

Experiment II. Twenty-one kittens were assigned to one of three groups (1) Perinatally-operated (KP; $\underline{N} = 7$); (2) Juvenile-operated (KJ; $\underline{N} = 5$); or (3) Unoperated control (KN; $\underline{N} = 9$).

The AO Ss were allowed two months of post-operative recovery prior to testing. The KP Ss were lesioned 14-16 days postpartum, and the KJ's at 119-121 days postpartum. For the kittens all behavioral testing commenced when the Ss were six months old.

Surgical procedures

All operations were performed aseptically while the animals were under anesthesia induced by sodium pentobarbital. The frontal gyrus was removed bilaterally by subpial aspiration. Post-operative recovery took place in an incubator held at a constant temperature of 80° F, during which time two liters of O₂/min. were administered to the KP Ss.

Histological procedures

When testing was completed, all operated Ss were administered a lethal intraperitoneal dose of sodium pentobarbital. They were then perfused intracardially with normal saline followed by 10% formalin. The brains were removed and, following graphic reconstruction of the lesions, were embedded in celloidin and sectioned at 30 μ . Every twentieth section through the lesioned area and every fifth section through the nucleus medialis dorsalis of the thalamus was saved and stained with cresylecht violet.

Cell loss, atrophy and gliosis were employed as the criteria for determining the extent of retrograde thalamic degeneration. Such degeneration was commonly observed in the middle of the nucleus medialis dorsalis between 11.0 and 8.0 mm. anterior in terms of the coordinates of

Jasper & Ajmone-Marsan (1960). The amount was comparable from cat to cat, though somewhat smaller than in the preparations studied by Warren, Warren, & Akert (1962).

The lesions were topographically equivalent to those of Lawicka & Konorski (1961). The poles of the gyrus proreus were always destroyed, but the ventrocaudal portions of the gyrus were occasionally spared. The lesions extended into the medial wall of the sulcus presylvius, but did not invade the ventromedial portions of the coronal gyrus.

Apparatus

Figure 1 presents a diagram of the equipment. From a central start box, each of three guillotine doors led to a runway and goal box. The runway and goal box were painted black, white, or gray; and these colors were continued into the center of the start box. An audio generator was connected in parallel through a push button and selector switch to speakers which were located in the apices of the triangle. A 1000~ tone of three seconds' duration was used as a signal.

Reinforcements (commercially prepared dried cat food pellets which were soaked in fish oil) were administered by hand through funnels and tubing which extended downward through 3/4" holes cut into the top of the goal boxes. During all phases of pretraining and training, the Ss were under 23 hours food deprivation.

Behavioral procedures

Pretraining. The Ss were habituated to the apparatus for 30 min., trained to eat in all of the goal boxes, trained to return to the start box after eating, trained to leave the start box when the doors opened, and then, for 60 trials, pretrained to eat in the presence of the tone.

Figure 1. Diagram of Apparatus

Training. A procedure modified from that used by Lawicka & Konorski was employed. (1) After S was in the start box, the tone was sounded for three seconds, all start box doors were opened simultaneously, and the tone was terminated. (2) If correct, the animal's response was reinforced with three pellets, and the doors to the other goal areas were closed; when the S re-entered the start box, that door was closed behind him. (3) If the initial choice was incorrect, all doors remained open, and the S was permitted a second choice which, if correct, was not reinforced; all start box doors were closed after the S re-entered the start box after the second choice. (4) After each incorrect trial, the same signal was presented on the subsequent trial and on each succeeding trial until a correct response was made.

All Ss were given 12 reinforced trials/day--4 reinforced trials to each goal box. The correct goal box for each trial was selected according to a predetermined order in which each goal box was correct twice within each of two successive blocks of six trials. Seven orders, used consecutively, were prepared. The intertrial interval was 15 sec. Criterion performance was two consecutive days on which the S made a maximum of only three errors/day and made 9 correct responses within a block of 10 trials.

Error analysis

Each error was sorted into one of four categories: perseverative, anti-perseverative, preference-omission, or unclassified. Perseverative errors are consecutive responses made to the last reinforced goal box on those trials where the correct response is to another goal box. An anti-perseverative error consisted of an incorrect response or series

of incorrect responses made between two correct responses which went to the same goal box. Preference-omission errors consisted of (1) two or more errors made between two correct responses each of which went to a different goal box and the first error in the chain was not a perseverative error; (2) two or more errors made at the start of each day's testing session; (3) within a chain of perseverative errors if the animal went to the third goal box (not a perseverative error or a correct response) then all succeeding errors were classified as preference-omission errors even if the animal began making perseverative errors within the same chain. Unclassifiable errors were any erroneous responses which could not be sorted into the above categories.

RESULTS AND DISCUSSION

Experiment I. Though animals with lesions sustained in adulthood (AO) required a median of 260 trials to reach criterion performance while the AN group score was 239, there was no significant difference between them. Median errors to criterion were fewer in the AN than in the AO group, but again the difference was not significant (83 versus 124). Neither group successfully corrected after having made a first-choice error on a trial: the AO Ss median was 49 per cent; the AN Ss median was 50.

Analyses of types of errors indicated that percentages of errors which could not be assigned into formal categories were about as frequent in both groups of animals (a median of 15 for the AO group, and of 19 for the AN group). Other errors showed a pattern, though a very weak one, of the sort observed by Lawicka & Konorski in their work with adult

frontal cats. The AO Ss tended to make more perseverative errors (23 compared with 17), but fewer of the anti-perseverative type (25 compared with 32). Further, the AO's made more errors classed as being due to preference-omission than did the AN's (here the AO median per cent was 37, as compared with 31 for the AN's). Inter-individual variability was such that these results were no more than suggestive, but a Mann-Whitney test supported the anit-perseverative difference ($U = 11.5$, $p < .05$).

Experiment II. To a point, results obtained from kittens paralleled the outcomes of the study done with cats. KP's, KJ's, and KN's all managed to attain criterion performance on the task, though they required approximately twice as many trials as either adult group (355, 571, and 521 respectively). Errors to criterion were also roughly twice as high as in the study with the cats (156, 246, and 192 respectively). Second-choice responses after errors were at chance, the median percentage values being 50, 53, and 50 for the KP's, KJ's, and KN's respectively.

Since the operated groups could not be told apart on any of the measures that were taken, they were next combined for a comparison between them and the KN animals. (KP and KJ median percentages of classified errors were 18 and 18 [perseverative], 20 and 29 [anti-perseverative], and 38 and 39 [preference-omission] respectively.) Groups thus formed resembled one another very closely with respect to several of the scores. For example, KP-KJ Ss reached criterion in a median of 549 trials, and KN Ss reached criterion in a median of 521 trials. Median errors to criterion were 192.5 for the KP-KJ Ss and 192 for the KN Ss. Errors not assigned to any formal class were 17 and 22 per cent.

Finally the median percentages of errors of perseveration were the same; this score was 18 for the KN group and was also 18 for the KP-KJ group.

Nonetheless, there were some striking differences between the groups in terms of certain kinds of errors. Thus the KP-KJ Ss tended to make errors which were classed as preference-omission: a median of 38.5 per cent, whereas the KN median was 27 per cent. This relation was reversed for errors classed as being of the anti-perseverative type: the KP-KJ median was 23 per cent, and that for KN Ss, 34. The latter difference has a p of $<.001$; the former of $<.03$, as determined by Mann-Whitney two-tailed estimations.

The question, then, is whether these results suggest effects of early operation which are different from the consequences of gyrectomies performed upon cats which have reached maturity. The answer seems to be that, in the present set of data, there is no support for such a view, even though the kitten outcomes were significant, or more so, than the ones with adults. Kittens made more errors, but the distribution of these errors and errors of adults were similar in normal and in operated groups regardless of the ages of the Ss. Thus, if we compare the KP-KJ with the AO, and KN with the AN groups (Table 1), the differences between the age groups are certainly less striking than the comparabilities of patterns.

The picture is consistent with contemporary concepts in that, after frontal operation, preference-omission errors tend to be more common than they are in normal cats and kittens. It should be recalled that these are errors which occur when Ss, having erred initially, do not repeat that error but will make a second error when confronted with the

other alleys. Inasmuch as errors of this type will be inflated by approach-avoidance biases, the fact that frontal lesions make them commoner in cats supports the Brush, Mishkin, & Rosvold (1961) result with monkeys. Further, we confirm, with a very different apparatus, changes of a kind which were observed in the initial three-choice study of the frontal cat conducted by Lawicka & Konorski (1961).

TABLE 1

Percentages of Errors by Groups

	AN	KN	AO	KP-KJ
Perseverative	17	18	23	18
Anti-perseverative	32	34	25	23
Preference-Omission	31	27	37	38
Unclassified	19	22	15	17

Operated Ss also tend to be less likely to commit an error than are normal animals when the error follows a correct selection and that alley is correct on the next trial (anti-perseverative errors). Since there is no increase in perseverative errors, we believe that this reduction comes from a reduced discrimination of the momentary probabilities of reinforcement. That is, when a given alley has been reinforced, that means that a choice of other alleys is more likely to produce a reinforcement than a repetition of the first selection. The efficient strategy, apart, of course, from going to the alley where the tone was sounded, is to choose between the alleys which had not been chosen and rewarded on preceeding trials.

Although we confirm Lawicka & Konorski's finding with respect to preference-omission, it could seem that our results deny their observation that the frontal perseverates. However, we would point out that the present situation differs rather markedly from theirs despite the fact that both investigation have employed a three-choice and an indirect procedure. In their work, a trial commenced when S was in a start box facing three alternative goal boxes, and their situation rather obviously favors execution of perseverative choices which depend upon the S's start box orientation. In our apparatus, cats and kittens may (and do) exhibit some perseverative responses; but to do this they must turn about, after having entered the start box, in order to reenter the same goal box. Accordingly, two factors seem to work against there being a perseveration of responses: (1) the probability that the same response will be rewarded; (2) mechanical considerations.

In summary, the outcomes seem to be consistent with the supposition that the frontal cat exhibits the same relatively strong approaches and avoidances observed in frontal monkeys. Second, they suggest impairment of the frontal cat's capacity to make discrimination of sequential changes in the probability of reinforcement of a given choice. Finally, impairments of these kinds do not appear to vary with the age at operation, and in that respect we may contrast them with impairments not found after early extirpations.

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