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THE EFFECT OF EXPERIENCE UPON OPERANT PERFORMANCE FOLLOWING CEREBELLAR LESIONS IN THE RAT

The Ohio State University Ph.D. 1984

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THE EFFECT OF EXPERIENCE UPON OPERANT PERFORMANCE
FOLLOWING CEREBELLAR LESIONS IN THE RAT

DISSERTATION

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

by
William Timothy Kirk, B.S., B.A., M.A.

** * * *

The Ohio State University
1984

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Publications

Kirk, W.T., D. Hothersall, & G.G. Berntson. The effects of
  paleocerebellar lesions on DRL performance in the albino rat.
  Journal of Comparative and Physiological Psychology, 1982, 96,
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INTRODUCTION

The involvement of cerebellar structures in the regulation and coordination of motoric functions is well documented and is clearly evident in the clinical consequences of cerebellar insult. Such consequences often include dysmetrias and asynergias related in large part to an inability to inhibit motor movements (Dow, 1961; Dow & Moruzzi, 1958; Holmes, 1917, 1939). In addition, the role of the cerebellum in motoric-functioning has been suggested to include the neural encoding and storage of well-learned motor acts. Such theories postulate that the cerebellum plays a critical role in the establishment and execution of learned motor sequences in a manner similar to cerebellar involvement in postural and reflex mechanisms. Thus it has been postulated that as motoric sequences become well practiced, the increasing coordination and automaticity of these acts is mediated by cerebellar plasticity (Eccles 1967, 1977; Fujita, 1982; Gilbert, 1973; Ito, 1974; Marr, 1969). Related to this latter suggestion is the finding that following establishment of the classically conditioned nictitating membrane response in the rabbit, cerebellar injury eliminates the conditioned response without impairing the unconditioned response (McCormick, Lavond, Clark, Kettner, Rising & Thompson, 1981; McCormick & Thompson, 1984; Lavond, McCormick & Thompson, 1984).
These data indicate that cerebellar injury may profoundly compromise learned behaviors without overtly disrupting their motoric basis.

A growing body of data now suggest that cerebellar structures may also play an important role in the control and elaboration of complex motivated behaviors (Berntson & Micco, 1976; Berntson & Torello, 1982; Dow, 1974; Lavond, McCormick & Thompson, 1984; Watson, 1978a). A number of highly organized behaviors including grooming, eating and attack may be elicited by electrical stimulation of the anterior cerebellum and rostral fastigial nucleus within what has classically been termed the paleocerebellum. These behaviors are not merely motor automata, since they evidence serial organization, goal-direction, and sensitivity to the stimulus features of the goal object (Berntson, Potolicchio & Miller, 1973; Berntson & Paulucci, 1979; Larsell, 1934, 1937; Reis, 1973; Watson, 1978b). Moreover such stimulation has motivational consequences as evidenced by the fact that animals will self-administer stimulation at many cerebellar loci from which complex behaviors can be elicited (Ball, Micco & Berntson, 1974). Paralleling these observations are the findings that lesions of the paleocerebellum can disrupt exploratory behavior, social interactions, and defensive responses, in the absence of overt motor deficits (Berman, Berman, & Prescott, 1974; Berntson & Schumacher, 1980; Berntson & Torello, 1982; Peters & Monjan, 1971; Watson, 1978a).

In view of these diverse cerebellar influences, it is likely that the cerebellum exerts control over the sequential integration of behavioral functions at all levels of organization, ranging from
relatively simple reflex acts to complex behavioral processes. Thus, extensive cerebellar injuries have been shown to impair performance in simple mazes, which is related in part to motor dysfunctions (Lashley & McCarthy, 1926; Thompson, 1974). In contrast, more restrictive cerebellar injuries selectively impair performance on mazes that require sequential alternations of left and right turns (Pellegrino & Altman, 1970). Similar deficits have been demonstrated in two-choice visual discrimination tasks (Buchtel, 1970; Davis, Watkins, Angermeler & Rubia, 1970). These deficits appear to result from an inability to inhibit responding, or to switch response strategies. Such behavioral sequelae are reminiscent of the motor deficit, dysdiadochokinesia, seen following cerebellar injury, but in these cases are manifest at a more global level of behavioral organization.

Previous investigation in this laboratory (Kirk, Berntson, and Hothersall; 1982) demonstrated that subjects with paleocerebellar lesions have a pronounced performance deficit when required to specifically withhold a previously established operant response in a differential reinforcement of low rates (DRL) schedule. This deficit, however, was overcome when an overt "collateral" behavior was made available. In light of these findings, it was suggested that the DRL deficit resulted from an inability to organize or sequence behaviors, rather than from a loss of timing ability or motoric dysfunction per se. The present studies were designed to explore this issue, to further characterize the nature of operant deficits following cerebellar injuries, and to further examine the specific cerebellar systems involved in these deficits.
EXPERIMENT 1

The cerebellum has vast anatomical and functional connections with virtually every level of the neuraxis. The anterior cerebellar vermis projects primarily to the fastigial nucleus, which in turn, provides both ascending and descending outputs. The descending projections, via the hook bundle of Russell, terminate heavily in the vestibular nuclei, brainstem reticular formation, and to a lesser extent the spinal gray matter (Brodal, 1981; Martin, King & Dom, 1974; Snider, Mati & Snider, 1976). Ascending fastigial fibers project via the superior cerebellar peduncle to multiple sites within the midbrain reticular formation, midbrain central gray, and nuclei of the extrapyramidal motor system. In addition, rostral projections terminate diffusely in the thalamus, hypothalamus, and diverse limbic areas (Anand, Malhotra, Singh & Dua, 1959; Angaut & Bowsher, 1970; Harper & Heath, 1973; Heath & Harper, 1974; Snider, 1975; Snider & Mati, 1976). The dentate nuclei provide the major rostral outflow of the cerebellum. This projection, via the superior cerebellar peduncle, projects heavily to extrapyramidal structures such as the red nucleus, basal ganglia, and to the ventral lateral nucleus of the thalamus, from which influences are radiated to widespread cortical areas (Brodal, 1981; Dow, 1961; Dow & Moruzzi, 1958; Modianos & Pfaff, 1976; Sprague & Chambers, 1959, Snider, 1967).
As described above, previous reports have indicated that cerebellar injuries result in behavioral performance deficits which are not secondary to motoric dysfunctions. In general, such deficits have been reported following lesions of the cerebellar vermis or the fastigial nuclei, within what has been classically been termed the paleocerebellum (Berntson & Torello, 1982; Watson, 1978b). In a previous study, Kirk, Berntson, and Mothersall (1982) reported a marked DRL performance deficit following injuries within the paleocerebellum. In order to replicate this finding, and more fully clarify the cerebellar systems involved in this deficit, the effects both paleocerebellar and neocerebellar injuries on DRL performance were examined.

Method

Subjects. Seventy-Two male albino rats (90-120 days of age) were obtained from Charles Rivers or were bred in the laboratory from the same strain of animals. Subjects were group housed and maintained under a 12-hour light/dark cycle with ad lib. food (Purina Lab Chow) and water.

Surgery. Surgery was performed under sodium pentobarbital anesthesia (55 mg/kg IP), following pretreatment with atropine sulfate (.12mg IP). Once fully anesthetized, each subject was secured in a Kopf stereotaxic instrument and the skull was exposed. Electrode coordinates (fastigial: AP -11.5, ML + 0.8 from the midline, DV -7.7 below the skull; dentate: AP -9.6, ML + 3.5, DV -4.5; vermal: AP -10.3, ML + 1.0, DV -6.0) were derived from the atlas of Finkova and Marsala (1967).
Trephine holes were then drilled, and a monopolar electrode insulated except for .5 mm at the tip was lowered to the appropriate sites. Bilateral electrolytic lesions were then induced (1.5 mA anodal DC current for 10 sec), the electrode was withdrawn, and the scalp incision was sutured. Control animals were anesthetized and mounted in the stereotaxic instrument, but received no further surgical manipulation. Following surgery animals were administered a broad spectrum antibiotic (Duracillin, 200,000 units) and were returned to individual home cages.

**Apparatus.** The apparatus consisted of 8 conventional operant chambers, each with a single bar, food well, and house light on the front wall. The chambers were isolated within individual sound attenuating chests, and white noise was used to mask extraneous sounds. Reinforcement schedules were programmed, and response measures recorded by an Apple microcomputer interface located in a room adjacent to the testing chambers.

**Procedure.** After twenty-one days of postoperative recovery, subjects were reduced to 85% of normal body weight and were maintained at this level throughout the remainder of testing. Training and test sessions were one hour in length and were conducted 6 days a week, between 10:00 AM and 7:00 PM during the light portion of the light/dark cycle. Using conventional operant techniques (Anger, 1956; Innis, Keberg, Mann, Jacobson & Turton, 1983; Innis, Simmelhag-Grant & Staddon, 1983; Slonaker & Hothersall, 1972), subjects were trained to bar press for appetitive reinforcement (45 mg Noyes pellet). After acquiring the operant response and earning 100 reinforcers, subjects were shifted to a
DRL 5sec schedule. Thereafter, when subjects earned ten reinforcers, the schedule interval was progressively increased by 5sec until a DRL 20sec schedule was attained. Behavioral testing continued for twenty-four sessions. The total number of responses emitted, the number of reinforcers earned, and the individual interresponse times (IRTs) were recorded for each session.

Histology. After the completion of all behavioral testing, subjects were sacrificed by an overdose of sodium pentobarbital, and were perfused intracardially with normal saline followed by 10% formalin. The brains were then removed, frozen with dry ice, and 50 μ sections were cut with a Reichert microtome. Every fifth section through the lesion was slide-mounted and stained with cresyl-violet. The locations and extents of the lesions were then plotted by direct projection (B&L tri-simplex microprojector) onto diagrams of Fifkova and Marsala (1967). In order to minimize error in the estimated lesion size due to shrinkage or distortion of the tissue over the long survival time employed, care was taken to draw lesion boundaries based on remaining tissue rather than acellular areas. Lesions were evaluated and then classified (fastigial, dentate, vermal) by a judge unaware of the behavioral data.

Results

Histological Results. Histological examination revealed that lesions were relatively restricted to the dentate nuclei and surrounding cortex of the neocerebellum, or were confined to the paleocerebellum, which includes portions of the anterior vermis and fastigial nuclei. In
order to evaluate any behavioral differences that might be due to the variance in the size or location of the lesion, quantitative measures of the extents of the lesions were obtained through planimetric analysis (K&E 620015 Compensating Polar Planimeter) of the standard lesion reconstructions. In addition, the dorsal-ventral, rostral-caudal, and medial-lateral centers of the lesions were also determined. Consistent with previous investigation (Kirk, Berntson, & Hothersall, 1982), analysis of these data failed to discern any ubiquitous pattern in the performance of animals with lesions of the anterior vermis, or its projection site, the fastigial nucleus. Further, analysis of the performance of subjects with such lesions again failed to show any differences between lesions of the fastigial nuclei and or lesions restricted to the anterior vermis \((T = .603, df = 22, P > .05)\). In view of these considerations, subjects with vermal and fastigial lesions were pooled for subsequent analysis. Figure 1 shows representative lesions of the histological groups.

**Behavioral Results.** All subjects with cerebellar injuries demonstrated marked motor impairments, including tremor and ataxia, especially of the hindlimbs. Consistent with previous reports (Berntson & Schumacher, 1980; Fish, Baisden, & Woodruff, 1979; Modianos & Pfaff, 1976), these overt motor impairments diminished rapidly and by the commencement of behavioral testing, 30 days after surgery, lesioned animals were virtually indistinguishable from normal animals.

Cerebellar lesions did not appear to impair subjects' ability to acquire the CRF barpress response for appetitive reinforcement. Lesioned
subjects and sham-operated controls required an average of three test
sessions to acquire the barpress response and earn 100 reinforcers on
the CRF schedule. When switched to the DRL task, however, differences
between subjects with lesions and controls became apparent. As
illustrated in Figs. 2 & 3, subjects with vermal/fastigial lesions
showed impaired acquisition of the DRL task, characterized by reduced
efficiency and elevated response rates, especially within the early
phases of the schedule interval. Subjects with lesions of the dentate
nuclei, however, showed essentially normal acquisition of the DRL task
with only small increases in response rate (see Figs. 2 & 3). Analyses
of variance revealed that while all groups showed a reduction in the
number of barpresses over training sessions ($F = 40.072$, df = 3, $P <
.001$; see fig. 3), groups differed significantly in the total number of
responses emitted ($F = 6.163$, df = 2, $P = .003$). Moreover, while all
groups showed improvement in the efficiency ratio with training, ($ER =
reinforcers/responses$, Kramer & Rilling, 1970) ($F = 58.123$, df = 3, $P <
.001$), there were again overall group differences on this measure ($F =
3.755$, df = 2, $P = .027$).

Interresponse time data (see fig. 4) revealed that animals with
paleocerebellar lesions evidenced maximal responding at intervals too
short to satisfy schedule requirements. In contrast, animals with
dentate lesions showed a normal IRT distribution. A two-way ANOVA on the
IRT distributions revealed that with continued training, all groups were
altering their response tendencies to fit the temporal contingencies of
the schedule ($F = 37.311$, df = 9, $P < .001$). However, there were again
lesion-related differences in the IRT distributions ($F = 2.947, df = 3, P = .038$). Further, there was a strong interaction between lesion and time-interval factors ($F = 2.699, df = 27, P < .001$) reflecting the failure of animals with fastigial/vermal lesions to suppress responses during the early phases of the DRL interval (see Fig. 4).

Planimetric analysis of the standard lesion reconstructions failed to reveal any consistent relationship between lesion size and DRL performance in either the dentate or the vermal/fastigial lesion group. Moreover, subsequent regression analysis between lesion size and terminal efficiency on the DRL schedule confirmed this result (dentate: R-squared = .08; vermal/fastigial: R-squared = .02).

**Discussion**

The overall pattern of results presented in this experiment is consistent with the report that paleocerebellar lesions result in a post-operative DRL deficit (Kirk, Berntson, & Hothersall, 1982). The present findings, however, also demonstrated that such deficits are specifically related to destruction of the anterior vermis and/or fastigial nuclei, and are not apparent after lesions of the dentate nuclei. The performance deficit was characterized by overresponding early in the schedule interval, together with a peak shift toward IRTs of shorter duration. Three possible explanations for the failure of lesioned subjects to redistribute their responses toward longer IRTs are that they are unable to appropriately time the schedule interval, are unable to inhibit responding, or are simply slower to acquire the schedule constraints.
EXPERIMENT 2

It has been argued that the development of "collateral behaviors" may serve to mediate timing of the schedule interval and thus improve timing performance (Hothersall, Alexander & Slonaker, 1972; Laties, Weiss, Clark, & Reynolds, 1965; Laties, Weiss & Weiss, 1969; Slonaker & Hothersall, 1972). In this regard, the explicit provision for a collateral behavior, through the introduction of a chewing block, has been shown to alleviate DRL deficits following cerebellar injury. The rapid improvement seen in these animals following introduction of the block suggests that their performance deficit is not simply the result of a learning deficit. While this improvement may be due to an enhancement of timing ability by the collateral activity, it is also possible that the collateral may provide a response competitor which serves to disrupt perseverative bar-pressing. According to this view, the DRL deficit may be due to an inability to inhibit responding. A related possibility is that the DRL deficit is due to a perseveration of response set or strategy, carried over from original CRF training. This latter argument suggests that subjects with cerebellar injury may be capable of performing well on the DRL schedule, but would acquire the schedule more slowly than controls on transfer from a CRF schedule.
This latter hypothesis may suggest that cerebellar lesions would have nominal effects in subjects which were well-trained on the task prior to receiving their injuries. To directly test this hypothesis, control subjects from experiment 1 were subsequently given paleocerebellar (fastigial) lesions and then retested on the DRL task. In addition, previously lesioned animals were again tested on the DRL task to assess the effects of long recovery times and extended training.

Method

Subjects. Subjects were the 37 control subjects from experiment 1.

Surgery. Fifteen of the normal control subjects from experiment 1 were given paleocerebellar lesions, and remaining subjects were sham-operated according to the procedures described in experiment 1.

Apparatus. The apparatus was that used in experiment 1.

Procedure. Upon completion of behavioral testing in experiment 1, control subjects were paired for previous performance and half were given paleocerebellar (fastigial) lesions. Matched controls were sham-operated in accordance with the procedures outlined above. After twenty-one days of post-operative recovery, subjects were reduced to 85% of normal body weight and were maintained at this level for the remainder of behavioral testing. Subjects were then given twelve additional test sessions on the DRL task using the procedures described in experiment 1.
**Histology.** Upon completion of all behavioral testing, experimental subjects were sacrificed and prepared for histological examination as described in experiment 1.

**Results**

**Histological Results.** Histological examination revealed that the anterior paleocerebellar lesions experimental subjects received were comparable in size and loci to those of the vermal and fastigial groups described in experiment 1 and illustrated in figure 1. Consequently, these lesions are not illustrated here.

**Behavioral Results.** Upon reintroduction to the test chambers, all subjects attained efficiency ratios equivalent to those reported at the end of experiment 1, but showed an increased response rate ($F = 9.194$, $df = 1$, $P = .003$, see Fig. 3). Consistent with the findings in experiment 1, lesion-related differences in response rates persisted ($F = 5.796$, $df = 3$, $P = .001$), due to the high response levels of subjects receiving paleocerebellar lesions prior to operant training (Newman-Keuls test on differences between all pairs of means $P > .05$). As illustrated in figure 2, however, all subjects continued to show increases in efficiency ($F = 59.275$, $df = 1$, $P < .001$) with concomitant reductions in responses ($F = 18.177$, $df = 1$, $P < .001$). With the additional testing significant group differences in efficiency disappeared ($F = .103$, $df = 3$, $P > .05$). However, while efficiency ratios of lesioned animals ultimately approached those of control subjects, inspection of the IRT distributions for the sixth week of DRL training (see Fig. 4) reveals
that subjects receiving cerebellar injuries prior to DKL training
continued to show an abnormal IRT distributions.

In contrast to these results, subjects receiving cerebellar lesions
following DKL training did not differ from sham-operated controls in
either efficiency ($F = .344, df = 1, P > .05$), response rate ($F = .228,
df = 1, P > .05$), or IKT distribution ($F = .628, df = 1, P > .05$; see
Fig. 2 & Fig. 3). These data suggest that DRL performance after
cerebellar lesions is partially recoverable, and that preoperative
training may offer some protection against the effects of subsequent
cerebellar lesions.

**Discussion.**

Results of this experiment indicate that preoperative training
greatly reduces the effects of subsequent cerebellar lesions. Moreover,
subjects receiving cerebellar lesions prior to training do improve in
efficiency following a protracted break and additional testing. However,
while efficiency ratios improve with extended training, animals not
having received preoperative training continued to show elevated
response rates and abnormal IRT patterns persist after extended operant
training. Thus their improvement appears to reflect an uniform decrease
in responding rather than the selective inhibition of responses early
within the schedule interval which is characteristic of intact subjects.

The high response rates shown by subjects with cerebellar lesions
do not appear to reflect a global deficit in inhibition of motor
responses. In that case one would expect a comparable deficit in
subjects given preoperative training. Rather, the present results are more consistent with the hypothesis that cerebellar lesions result in a deficiency in altering a response set or strategy. Consequently, animals with cerebellar lesions continue to respond in a manner inappropriate to the DKL schedule.
EXPERIMENT 3

Results of the previous experiments suggest that the DRL deficit seen following paleocerebellar lesions results from a perseverative increase in responding, especially within the early phases of the schedule interval. In addition, these results suggest that this deficit is not reflective of a global disruption of the ability to suppress responding, since animals pretrained on the DRL task, prior to cerebellar injury, perform normally. It is not clear, however, whether this deficit results from a timing deficiency or from the perseverative use of a response strategy acquired during CRF pretraining. In order to directly investigate these possibilities, animals with fastigial lesions and sham-operated controls were trained on either a DRL or fixed interval (FI) schedule. Both of these tasks permit a test of timing ability, but each requires a different response strategy for optimal performance. Thus, if lesioned subjects suffered timing deficits, they should demonstrate not only poor DRL performance, but would be inefficient on the FI task as well. In addition, subjects were shifted from one schedule to the other to permit an assessment of potential perseveration of response strategies.
Method

**Subjects.** Twenty-four male albino rats (90-120 days of age) were obtained from Charles Rivers or were bred in the laboratory from the same strain of animals. Subjects were group housed and maintained under a 12-hour light/dark cycle with ad lib. food and water.

**Surgery.** Twelve animals were given cerebellar lesions and remaining animals were sham-operated according to the procedures outlined in experiment 1.

**Apparatus.** Apparatus was that used in experiment 1 and described above.

**Procedure.** Subjects were reduced to 85% of normal body weight following 21 days of postoperative recovery and were maintained at this level for the remainder of behavioral testing. Training and test sessions were one hour in length and subjects were trained to barpress for appetitive reinforcement according to the procedures described in experiment 1. After subjects acquired the operant response and earned 100 reinforcers on a CRF schedule, subjects were shifted to either a DRL or FI 5sec schedule. Both schedules provide a test of a subject's ability to accurately time a specified interval; the DRL schedule, however, specifically requires that subjects withhold responding for the duration of the schedule interval. After subjects earned ten reinforcers, the schedule interval was progressively increased until either a DRL or FI 20sec schedule was attained. Behavioral testing continued for twenty-four additional test sessions (4 weeks), after which subjects were again permitted ad lib. access to food. In order to
permit direct comparisons between subjects in the present experiment and those in the previous experiments, all subjects were sham-operated according to the procedures outlined in experiment 1. Following 21 days of postoperative recovery, subjects were again reduced to 85% of their ad lib. body weight. Subjects were then reintroduced to the testing chambers and given 12 test sessions on the alternate schedule. Total responses emitted, reinforcers earned, and interresponse times were recorded for each test session.

Histology. Following the completion of all behavioral testing, subjects were sacrificed and prepared for histological examination according to the procedures described in experiment 1.

Results

Histological Results. Experimental subjects were found to have lesions of the paleocerebellum that were comparable to those from the vermal/fastigial group described in experiment 1 and illustrated in fig. 1. Consequently, these lesions are not illustrated here.

Behavioral Results. All subjects readily acquired the barpress response for appetitive reinforcement requiring an average of three test sessions to learn the operant and earn 100 reinforcers on a CRF schedule. Inspection of figure 6 reveals several striking differences between the schedules and the order in which they are experienced. In general, both lesioned and control subjects responded at much higher rates on an FI schedule than on a DRL schedule. It is interesting to note that while lesioned animals, regardless of schedule order, made
more responses on the DRL schedule than controls ($T = 1.727, df = 22, P < .05$), they tended to respond less than intact subject on the FI schedule. Moreover, while previous FI experience does not obviously affect subsequent levels of responding upon DRL, the reverse does not appear to be the case. Lesioned animals continue to emit low rates of responding when shifted from DRL to FI. These data are further confirmation of the results presented in experiment 1; when lesioned animals received initial training on the DRL schedule, they performed poorly. In contrast, when animals with such lesions were initially trained on FI and then switched to the DRL schedule they performed similar to intact animals with the same operant history. It was postulated above that the poor DRL performance of animals with paleocerebellar lesions might be due to a deficit in timing ability. The timing ability of subjects with cerebellar lesions on FI, however, appears good. Lesioned animals did not differ from normals in either median response time (lesioned animals: 17.6 sec vs 17.5 sec for controls) or in the dispersion of responses as indicated by the kurtosis of the response distributions (3.44 vs 3.88). A three-way ANOVA (SURGERY X ORDER X SCHEDULE) on median response times confirmed this observation ($F = 3.414, df = 1, P > .05$). A significant interaction between surgical and schedule factors ($F = 4.421, df = 1, P > .046$), however, indicates that the operant deficits of animals with paleocerebellar lesions were restricted to the DRL schedule (lesioned subjects: 14.6 sec vs controls: 19 sec). These findings suggest that the DRL deficit following cerebellar lesions is not due to a global deficit in timing ability per se.
As suggested above, it is possible that perseveration might account for lesion-related differences in DRL performance. The results of the present study support the conclusion from experiment 2, that this perseveration does not result from a general deficit in motor inhibition. If such perseveration were due to a global motoric deficit, one would expect animals with cerebellar injuries to consistently emit more responses than controls. A three-way ANOVA on responses, however, failed to reveal any such surgical effect ($F = 0.347, df = 1, P > .05$). Moreover, as is apparent in figure 6 subjects with cerebellar injuries showed lower response rates on the FI schedule than did normal animals. Further, lesioned animals which were initially trained on the DRL task emitted fewer responses on the subsequent FI task than did either normal animals or lesioned animals initially trained on the FI schedule. While the efficiency ratio is not conventionally employed for measuring FI performance, it does provide a means of estimating the effects of the punishment contingency upon response rate. A three-way ANOVA on this measure confirmed that previous DRL experience resulted in more efficient FI performance ($F = 7.893, df = 1, P = .01$). These findings support the view that DRL deficits following cerebellar injuries are due to perseveration of response strategies, rather than a global deficit in response inhibition.

The ability of animals with cerebellar lesions to perform well on a FI but not a DRL schedule is clearly reflected in the distribution of responses within the schedule interval (see fig. 6). Further the sharp, and appropriately timed response peaks evident in these distributions
for the FI schedule argue against the hypothesis that cerebellar injuries result in timing deficits. In view of the strong order effect revealed above, initial analyses on the response distribution data were performed separately. When a two-way ANOVA was performed on these data for subjects receiving initial FI training, it was confirmed that they responded differentially during schedule intervals \( F = 32.203, df = 9, P < .001 \); there were significant differences between distributions for the schedules \( F = 30.103, df = 1, P < .001 \) as well as a strong interaction between schedule and the temporal distribution of responses \( F = 26.672, df = 9, P < .001 \). Again, a similar pattern was found for subjects with initial training upon the DRL schedule. Subjects distributed their responses in accordance with the temporal dynamics of the schedules \( F = 19.275, df = 9, P < .001 \) and subjects again responded differently on the two schedules \( F = 9.015, df = 1, P = .016 \). Once again, there was a strong interaction between the schedule and temporal factors \( F = 10.084, df = 9, P < .001 \).

To more fully contrast the effects of order and schedule, response distributions were transformed to cumulative distributions, and a suppression index, designed to provide a quantitative measure of departure from a uniform response rate throughout the schedule interval, was calculated (Fry, Kelleher & Cook, 1960; see fig. 7). This transformation of the data tends to reduce the effects of higher response rates within the earliest portion of the schedule interval permitting a more direct comparison selective response suppression within the interval across schedules. A three-way ANOVA on the suppression indices
revealed that there were significant differences between the response patterns of intact and lesioned subjects ($F = 4.353$, $df = 1$, $P = .047$) and confirmed differences between the schedules ($F = 95.003$, $df = 1$, $P < .001$). Moreover, as shown above, the order of schedule presentation ($F = 8.647$, $df = 1$, $P = .008$) was found to affect response distributions, reflecting the modest increase in responding late in the interval on the FI schedule following DRL training. Further, an interaction between these effects ($F = 4.29$, $df = 1$, $P = .049$) suggests that lesioned animals may not switch schedules as readily as the overall response measures indicate.

Discussion. It has been postulated that the DRL deficit seen following cerebellar injury may result from poor timing ability or an inability to inhibit responding, possibly reflecting some underlying motoric dysfunction. The performance of lesioned animal on a FI schedule, however, clearly demonstrates that they are capable of accurately judging the schedule interval. If cerebellar injuries resulted in a timing deficit, one would expect either a shift in the response distribution toward shorter intervals, or a flattening of IRT peak. The results in the present study failed to reveal any differences in FI performance or the distribution of responses between lesioned and control subjects when they were initially trained on this task.

One of the characteristic features of the DRL deficit, is an increased numbers of responses. The absence of overresponding on the FI schedule, however, indicates that this DRL deficit is not merely reflective of a global deficit in response inhibition.
EXPERIMENT 4

The preceding experiments demonstrate that animals with paleocerebellar injuries emit more responses early in the schedule interval than controls when tested on a DRL task. This deficit is not apparent when subjects are preoperatively trained on a DRL schedule. It was suggested above that the deficit reflects the perseverative use of an inappropriate response strategy. This occurs in spite of a specific schedule contingency against high response rates. Previous studies have demonstrated that cerebellar lesions can have emotional consequences, and specifically that lesions of the fastigial nuclei can greatly attenuate the emotional effects of septal injuries (Berntson & Torello, 1980) while lesions of the vermal cortex can reduce levels of aggressive behaviors (Chambers & Sprague, 1955; Peters & Monjan, 1971). In light of these findings, it is possible that the increased levels of responding on the DRL task following cerebellar injuries may result from a decrease in the inhibitory reactions to the aversive qualities of unreinforced responses. To explore this possibility, subjects from the preceding experiments were tested for reactivity to a startle stimulus and for the inhibitory effect of a very weak preliminary stimulus (prepulse inhibition) on startle reactivity.
**Method**

**Subjects.** Subjects were 28 lesioned and 19 sham-operated subjects used in the preceding experiments.

**Apparatus.** Apparatus consisted of a small cage (200mm X 120mm X 80mm) mechanically coupled to a speaker so that movements of the cage resulted in displacement of the speaker coil and the generation of a potential proportional to that voltage. This voltage was amplified and peak values measured by means of a pair of operational amplifiers configured as a sample and hold circuit.

**Procedure.** The startle reflex was elicited by a 20 millisecond burst of 108 DB white noise. The inhibitory stimulus consisted of an identical stimulus at 60 DB presented 60 milliseconds prior to the startle stimulus. Test sessions were preceded and followed by two presentations of the inhibitory stimulus alone in order to evaluate any possible response to this stimulus alone. Each subject received twenty-four presentations of the startle stimulus, twelve of which were preceded by the inhibitory stimulus. These were presented in a counterbalanced order with a one minute intertrial interval.

**Behavioral Results.** None of the subjects showed a measurable response to the presentation of the inhibitory stimulus alone, while all subjects showed a notable startle response to one or more of the presentations of the startle stimulus. Inspection of figure 8 reveals that while there were large differences in reactivity to the startle stimulus, both groups demonstrated almost no reactivity to the startle stimulus when it was preceded by the inhibitory prepulse. Analysis of
variance revealed that subjects with cerebellar lesions were less reactive than controls ($F = 5.224$, $df = 1$, $P = .030$). There was also a significant interaction between surgical and stimulus factors ($F = 4.177$, $df = 1$, $P = .05$), indicating a potential difference in the effects of the inhibitory stimulus. The interpretation of this interaction, however, is confounded by the virtually complete suppression of the startle response by the prepulse stimulus in both groups.

It is possible that the attenuated startle reactivity is due to a motor impairment which precludes the sudden movements associated with the startle response. In order to address this issue and further characterize the nature of the startle attenuation, the group probabilities of a startle response to the startle stimuli were compared. Analysis on this measure revealed that while all animals startled at least once to the startle stimulus, lesioned animals showed not only a startle response of reduced magnitude, but also a significantly lower probability of a startle response (lesioned animals: 24% vs. 45% for the controls; $T = 2.121$, $df = 46$, $P = .037$).

Discussion.

Consistent with previous reports on the impact of cerebellar injuries on emotional responsiveness (Berntson & Torello, 1980; Chambers & Sprague, 1955; Peters & Monjan, 1971), subjects with rostral vermal and/or fastigial lesions were found to show a greatly attenuated startle response compared to controls. Moreover, this reduced startle reactivity
did not appear to be related to motor impairments which merely reduced
the response magnitude. Rather, the differences in reactivity following
cerebellar lesions appear to result more from a reduction in the
frequency of the startle response. Both normal and lesioned subjects
evidenced a greatly reduced startle response, when the startle stimulus
was preceded by an inhibitory prepulse stimulus, indicating that
cerebellar lesions do not attenuate the inhibitory effects of a prepulse
Lesions of the rostral vermis and/or fastigial nuclei produced a marked performance deficit when subjects were subsequently tested on a DRL 20sec schedule. This deficit was characterized by an increase in response rate sufficient to preclude efficient performance. Further, lesioned animals not only emitted more responses than intact subjects, they demonstrated abnormalities in the temporal patterning of their responses. This finding confirms the previous report of such deficits following cerebellar injuries (Kirk, Berntson, & Hothersall, 1982), and is consistent with a wider body of data indicative of cerebellar involvement in the elaboration and organization of behavior (Berntson & Torello, 1982; Watson, 1978a). In contrast, lesions of the dentate nuclei did not produce any appreciable alterations in performance.

The fastigial nucleus projects, via the superior cerebellar peduncle to a variety of structures within the diencephalon, limbic system and forebrain: including the amygdala, hypothalamus, septal area, hippocampus, and thalamus (Anand, Malhotra, Singh & Dua, 1959; Angaut & Bowsher, 1970; Harper & Heath, 1973; Heath, Dempsey, Fontana & Meyers, 1978; Heath & Harper, 1974; Whiteside & Snider, 1953). In addition, a number of less direct connections via the ventral tegmental area, periaqueductal gray, interpeduncular nucleus, substantia nigra, and the
catecholamine-containing neurons of the locus coeruleus suggest widespread fastigial influence in limbic and basal forebrain structures (Crutcher & Humbertson, 1978, Jacobowitz & McLean, 1978, Snider, 1975; Snider & Matiti, 1976; Snider, Matiti & Snider, 1976). Many of these projection sites have been shown to be involved in behavioral processes. Previous studies have reported DRL deficits after lesions of fastigial projection sites. For example, septal lesions result in a DRL deficit with very many parallels to the features of deficits following cerebellar lesions (Kirk, Berntson & Hothersall, 1982).

While the deficit seen following septal injuries appears relatively permanent, paleocerebellar lesions did not prevent the ultimate development of efficient DRL performance. With extended training on the task, lesioned animals were ultimately able to reduce excessive response rates sufficiently to perform at levels approximating normal performance. In spite of these improvements in performance, however, there remained a characteristic residual disturbance in number and distribution of responses within the schedule interval.

In contrast, operant performance on a FI schedule was unimpaired, and lesioned animals showed greater efficiency than did normals with a similar operant history on this schedule. The lower number of responses emitted by lesioned animals on the FI task, together with the accuracy of their timing performance, indicates that cerebellar lesions do not produce a global deficit in timing ability nor a pervasive inability to inhibit responding. Rather, results of the present study suggest that paleocerebellar injuries result in a deficiency in altering response
strategies and in the perseverative intrusion of the response set developed during prior training (e.g. CRF). Consistent with this suggestion was the finding that previous experience on the DRL task provides protection against the DRL deficit seen following cerebellar lesions. Moreover, when subjects were shifted from the DRL to the FI schedule, subjects behaved as if the more restrictive DRL schedule were still operative. Thus previous experience with a schedule which specifically punishes high response rates results in a continued lower rate of responding. This effect is most apparent in the almost complete suppression of responses within the early phases of the FI schedule interval (see fig. 7) by lesioned animals following initial DRL training.

Cerebellar lesions have been previously shown to result in a decrease in emotional responsiveness (Berman, Berman, & Prescott, 1974; Berntson & Torello, 1980, 1982; Peters & Monjan, 1971). In light of these findings, it is possible the DRL deficit may reflect in part a reduced responsiveness to the punishment contingency of the DRL schedule. Consistent with this possibility is the finding that subjects with cerebellar injuries are less responsive to a startle stimulus than are controls. While this finding is consistent with the notion that cerebellar lesions may diminish the effectiveness of the aversive consequences following short IRTs on a DRL schedule, it does not require such a conclusion or provide specific evidence in support of this proposition. A reduction in responsiveness to acoustic stimuli does not necessarily demonstrate a decrement in the effectiveness of other
negative reinforcers. Moreover, it would not account for the greater response inhibition evidenced on the FI schedule by animals with cerebellar lesions.

At present, the most plausible explanation of the DRL deficit appears to be based on an inability to adequately suppress responses within the early phases of the schedule interval, related in part to an impaired ability to switch response strategies. Preoperative training would permit subjects to acquire an appropriate response strategy prior to cerebellar injury. These animals need only to emit previously learned behaviors in order to perform well on the schedule.

The pattern of results presented here is consistent with previous reports describing deficits on a number of behavioral tasks related to lesions of the cerebellum (Berntson & Torello, 1982; Watson, 1978a). Moreover, a reexamination of these results in light of the present findings suggests that perseveration of response strategies may account for many of these deficits. Pellegrino and Altman (1979) reported a deficit in maze learning when subjects were required to alternate left and right turns. In this study, maze testing followed pretraining in a series of mazes designed to test position habits. While both experimental and control subjects showed good acquisition of the initial maze task, lesioned animals were demonstrably impaired when subsequently shifted to an alternation task. In the initial task lesioned animals could perform normally, when solution of the mazes required a spatial strategy. However, when the alternation task was introduced, which required the transition to the new strategy, lesion-related deficits were revealed.
Perseveration of response strategy is also consistent with the report that animals with cerebellar lesions demonstrate impaired extinction of a visual discrimination task (Rubia, Angermeier, Davis & Watkins, 1969; Davis, Watkins, Angermeier, and Rubia, 1970).

In summary, the behavioral data presented support a growing recognition in the literature that the concept of cerebellar functioning should be expanded to include not only the elaboration and sequential organization of motor acts, but of more complex behavioral performance as well.
Figure 1:

This figure presents representative dentate, vermal, and fastigial lesions.
Figure 2:

This figure presents efficiency ratio (reinforcers/responses) performance measures obtained during four weeks of acquisition training for subjects with vermal/fasigial lesions (inverted & closed triangles), dentate lesions (closed triangles), and sham-operated controls (open circles). In addition, efficiency data following a 30 day break in training are presented; subjects receiving vermal/fastigial lesions following behavioral training (closed circles) are included for weeks 9 & 10.
Figure 3:

This figure presents response measures obtained during four weeks of acquisition training for subjects with vermal/fasigial lesions (inverted & closed triangles), dentate lesions (closed triangles), and sham-operated controls (open circles). In addition, response measures following a 30 day break in training are presented; subjects receiving vermal/fasigial lesions following behavioral training (closed circles) are included for weeks 9 & 10.
Figure 3.

[Graph showing responses over weeks]

<table>
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<th>RESPONSES</th>
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<td>300</td>
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[Legend or symbols not clearly visible]
Figure 4:

This figure presents distributions of interresponse times for weeks 4 (solid lines) and 10 (dashed lines) for sham-operated controls (SS), for subjects with dentate lesions (DS), for subjects with fastigial lesions (FS), and for subjects receiving fastigial lesions after operant training (SF).
Figure 4.
Figure 5:

This figure presents response measures for subjects with fastigial lesions (dashed lines) and sham-operated controls (solid lines) on fixed-interval (FI) and differential reinforcement of low rates (DRL) schedules. Symbols denote schedule order: FI to DRL (closed triangles) and DRL to FI (closed circles).
Figure 5.
This figure presents the distribution of responses within the schedule interval for subjects with fastigial lesions (dashed lines) and sham-operated controls (solid lines) for weeks 4 and 10 of behavioral testing on fixed-interval (FI) and differential reinforcement of low rates (DRL) schedules.
Figure 6.
Figure 7:

This figure presents cumulative distribution of responses within schedule intervals for subjects with fastigial lesions (dashed lines) and sham-operated controls (solid lines) for weeks 4 and 10 of behavioral testing on fixed-interval (FI) and differential reinforcement of low rates (DRL) schedules.
Figure 7.

CUMULATIVE RESPONSES

CUMULATIVE RESPONSES

4 SEC BINS

4 SEC BINS

DRL

FI

DRL

FI
Figure 8:

This figure presents acoustic startle measures following presentation of a 20 msec., 108 DB white noise burst either alone (S) or paired with a 20 msec., 60DB white noise burst (PS) for subjects with fastigial lesions and sham-operated controls.
Figure 8.
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