Title

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Journal

Behavioral biology, 12(2)

ISSN

0091-6773

Authors

Smith, R L
Parks, T
Lynch, G

Publication Date

1974-10-01

Peer reviewed

BEHAVIORAL BIOLOGY, 12, 177-198 (1974), Abstract No. 3225

A Comparison of the Role of the Motor Cortex in Recovery from Cerebellar Damage in Young and Adult Rats[1]

REBEKAH L. SMITH, THOMAS PARKS[2]
and GARY LYNCH

*Department of Psychobiology, University of California,
Irvine, California 92664*

These experiments compare the motor development of rats with hemicerebellectomies performed at 10, 15, or 21 days of age. In addition, the effects of secondary motor cortex lesions are contrasted in these young-lesioned groups and in adults with similar cerebellar damage after the same post-operative interval. Of the young-lesioned groups, the 10-day operates showed the longest persistence of cerebellar symptoms, while the 21-day animals recovered normal motor patterns most quickly. The adult operates were also comparatively slow to eliminate motor behaviors characteristic of cerebellar damage. Following secondary bilateral motor cortex ablation, the greatest reinstatement of cerebellar symptoms occurred in the 10-day group, while the 21-day animals and adults were the least affected. These results are discussed in terms of possible mechanisms of functional recovery in the young and adult groups.

INTRODUCTION

In studies involving functional recovery from damage to the central nervous system, a common variable known to influence the rate and extent of compensation is the age of the subject at the time of surgery (see Rosner, 1970 for a review). Often operations in infants produce less debilitating or less persistent deficits than similar lesions in adults (Kennard, 1938 and 1942; Tucker, Kling and Scharlock, 1968; Goldman, Rosvold and Mishkin, 1970; Hicks and D'Amato, 1970; Schneider, 1970; and many others). However, in at least one case (Hicks, D'Amato, Klein, Austin and French, 1969), neonatally-

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[1] Research supported by grant GB 35315X from NSF, and grants MH 19793-02 and MH 11095-07 from NIMH. We would like to thank Christine Gall for her assistance in testing the animals used in this study.

[2] Present address: Department of Psychology, Yale University, New Haven, Connecticut 06520.

lesioned animals actually showed less recovery than the adults with similar brain damage. While the mechanisms underlying recovery are probably different depending on the brain systems damaged, a thorough age-dependent analysis of the changes in related undamaged systems may provide a better understanding of the comparative effects of, and mechanisms underlying, recovery from lesions in young and adult animals.

The cerebellum is well-suited for such an age dependent analysis of recovery. Many of the behavioral deficits which arise from cerebellar damage show remarkable recovery over time, whether following irradiation (Hicks *et al.*, 1969; Altman, Anderson and Strop, 1971; Anderson and Altman, 1972; and others) or ablation (Carrea and Mettler, 1947; Batini and Pompeiano, 1957; Sprague and Chambers, 1959; Smith, Mosko and Lynch, 1974). In addition, the neural substrates involved in cerebellar compensation in adults have been explored by several authors (see Smith *et al.*, 1974). The present study attempts to investigate and quantify: (1) the effect of hemicerebellectomy at three young ages on subsequent maturation of motor and postural behaviors; (2) the effect of similar lesions on the same aspects of behavior in adults; and (3) the relative significance of the motor cortex in compensation for early and adult cerebellar damage.

EXPERIMENT 1

Methods

A total of 80 male and female rats of the Sprague-Dawley strain were divided into four groups: 12 animals served as sham operates; 25 animals were lesioned at 10 days of age; 20 animals were lesioned at 15 days; and 18 animals were lesioned at 21 days. The older animals were operated under Nembutal anesthesia, with supplemental ether as needed; the 10-day operates received ether only. In all experimental animals the right half of the cerebellar cortex and underlying deep nuclei was aspirated with the aid of a dissecting microscope, using sterile procedures. The cavities were filled with Gelfoam moistened with an antibacterial solution of benzalkonium chloride. Sham operated animals were anesthetized and the scalp incised only. Skin flaps were glued with alpha cyanoacrylate rapid-bonding adhesive (10-day and 15-day groups) or sutured (21-day), and animals returned within 30 min to standardized litters of 6 pups per mother. Animals were separated from their mothers at 25 days and housed in pairs until 60 days old, at which time they were transferred to individual cages.

Testing was begun on all surviving animals two days following cerebellar ablation. Tests were conducted approximately every 5 days until age 30 days, and thereafter every ten days to age 70 days. Three classes of tests were used, based on some of those used by Altman *et al.* (1971), and by Lipton (1966):

(1) open field activity; (2) clinging to and descending a suspended rope; and (3) balancing on and traversing a narrow, elevated beam. Open field parameters included frequency of pivoting, falling, and dragging a hindlimb during locomotion, frequency of sitting without aid, standing with or without aid, and number of line crossings in a 3-min period. The activity box measured 30 × 30 cm, divided in 16 squares, with opaque walls 20 cm high. Animals were allowed to explore freely for two 3-min trials, separated by the rope and beam tests. Test periods on the rope and beam consisted of three trials each. Animals were placed head up with the belly against a 3 cm diameter stiff rope 50 cm from ground level. Normal rats cling to the rope at a young age; older animals are able to turn around and descend the rope. The time spent clinging to the rope (up to 60 sec) was measured, as were the frequency of falling off, the time to descend, and the percent descending. Activity on a smooth, 5 × 60 cm elevated beam was measured in frequency of falling off, total time on the beam (up to 60 sec), time to cross the beam, and percent crossing the beam successfully.

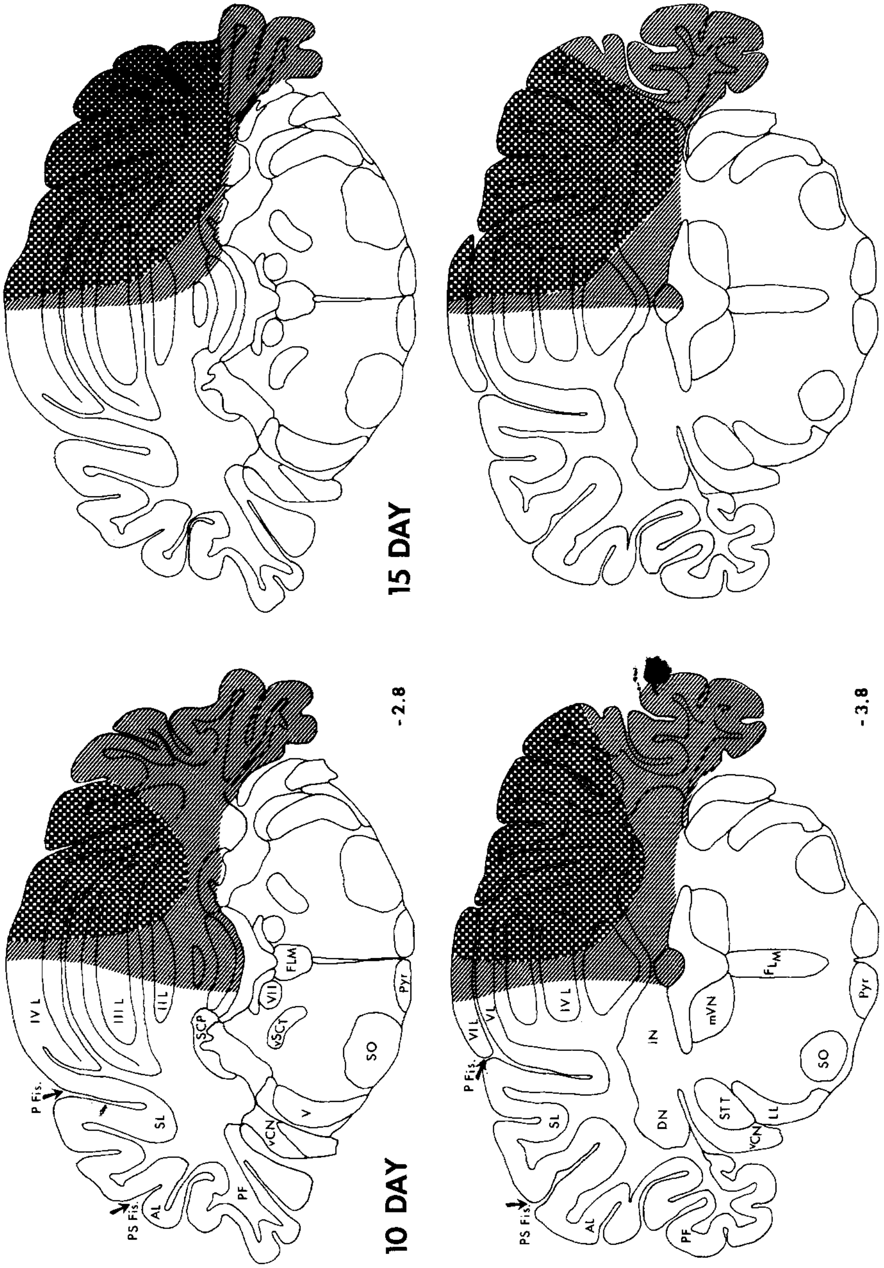
An additional test was performed on all animals at 60-69 days of age. This consisted of allowing the rats to run spontaneously down a darkened, plexiglas alley. This alley measured 12 × 90 cm, and was lined with touch circuits 10 cm apart along both lengths. The number of contacts with either side was noted for each of three trials in all animals. This measure was used as a test for postural or locomotor asymmetry.

Histological procedures are described in Expt 3. All statistical comparisons are based on a Mann-Whitney U test, except for alley scores, which were compared by a *t*-test.

Results

In the 10-day lesion group, seven animals died following or during surgery. Six others of the 15-day group, and four of the 21-day group also died. Following testing, histological analyses of the brains of the remaining animals indicated that four 10-day, six 15-day, and five 21-day animals suffered additional lesion damage to the dorsal brainstem. Only those animals which had no brainstem damage will be discussed or included in the statistical analyses of this study. Representative minimal and maximal cerebellar damage for each age group are presented in Fig. 1. As is apparent from the figure, all animals had nearly complete hemicerebellectomies. A few animals had some tissue remaining in the medial fastigial nucleus; however, the extent to which fiber connections of this area were intact could not be determined. Lesions were generally comparable among all groups, except that the minimal damage in the 10-day group was slightly smaller than in the other groups.

Weight curves over the period of testing were comparable for all four groups. None of the experimental groups differed significantly from controls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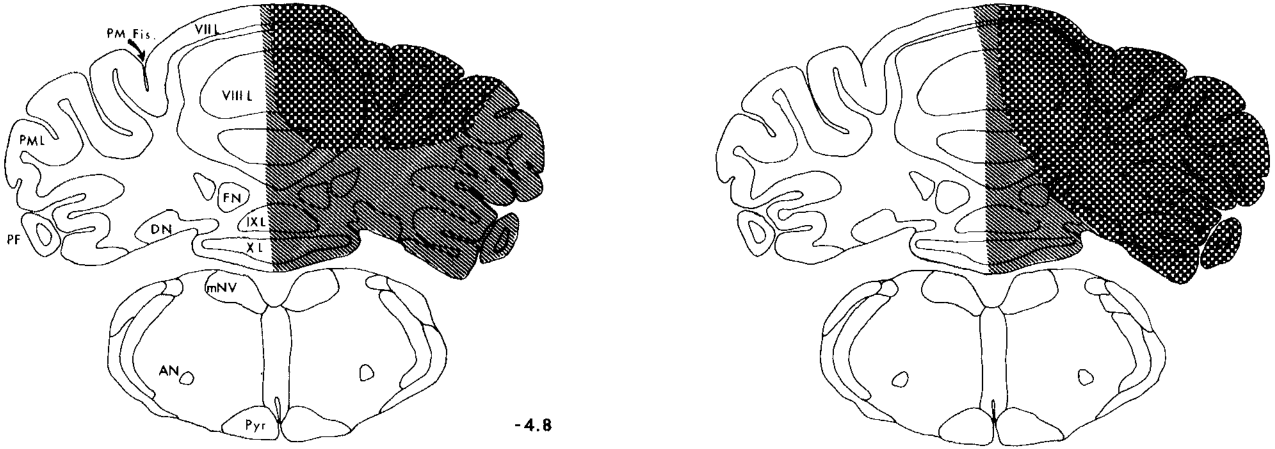
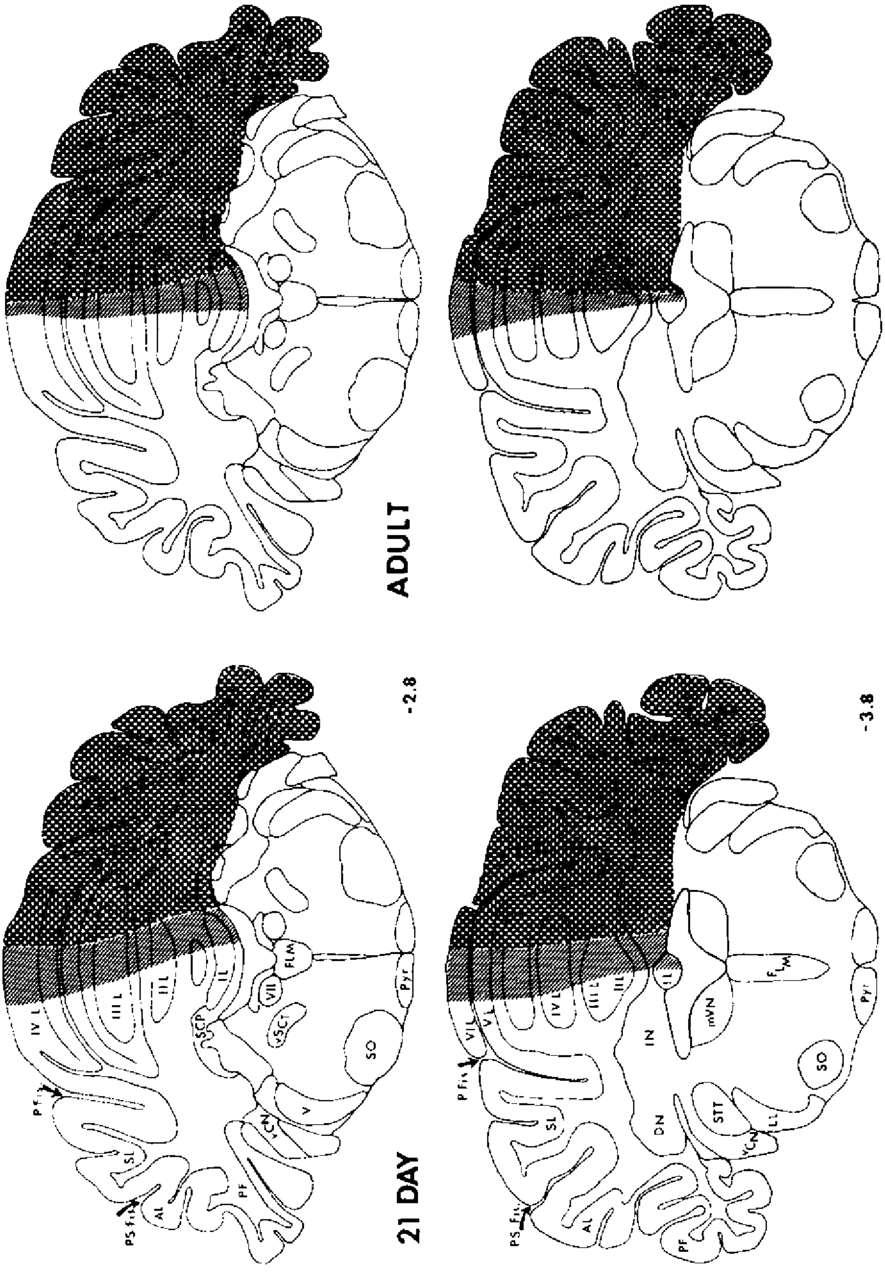


Fig. 1. Representative coronal reconstructions of minimal (checked) and maximal (striped) cerebellar lesions of four age groups at three anterior-posterior planes (approximately –2.8, –3.8, and –4.8) from interaural "0"). For 10-day group, $N = 14$; for 15-day group, $N = 8$; for 21-day group $N = 9$; for adult group, $N = 6$. (See following pages for 21-day and adult group.) Key to abbreviations in Fig. 1: AL–Ansiform lobe of cerebellum; AN–Nucleus ambiguous; DN–Dentate nucleus; FLM–Medial longitudinal bundle; FN–Fastigial nucleus; FNL–Flocculonodular lobe of cerebellum; ICP–Inferior cerebellar peduncle; IN–Interpositus nucleus; LL–Lateral lemniscus; IVN–Lateral vestibular nucleus; mVN–Medial vestibular nucleus; PF–Paraflocculus; P FIS–Prime fissure; PMFIS–Paramedian fissure; PML–Paramedian lobe of cerebellum; PS FIS–Posterior superior fissure; Pyr–Pyramid; SL–Simple lobe of cerebellum; SO–Superior olive; STT–Spinal tract of the trigeminal nerve; vCN–Ventral cochlear nucleus; vSCT–Ventral spinal-cerebellar tract; V–Trigeminal nerve; VII–Facial nerve; I-X–Cerebellar lobules according to Larsell (1952).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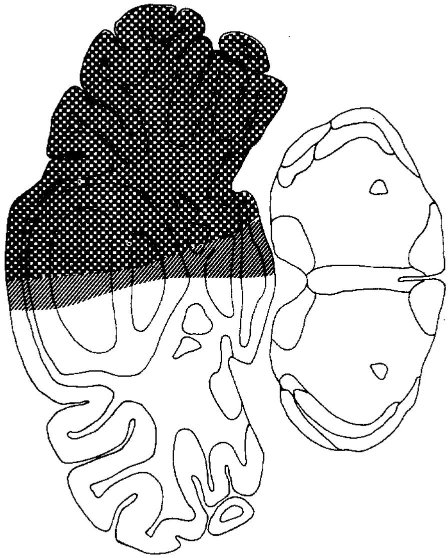

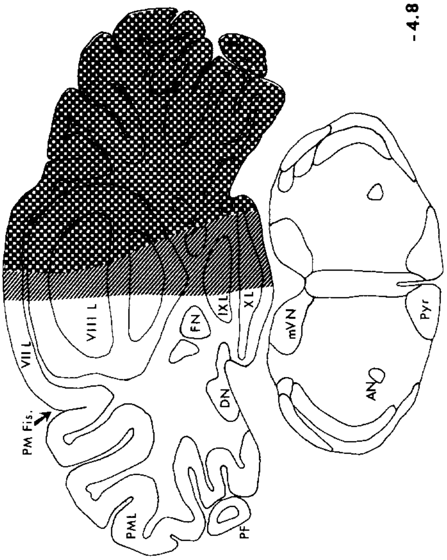
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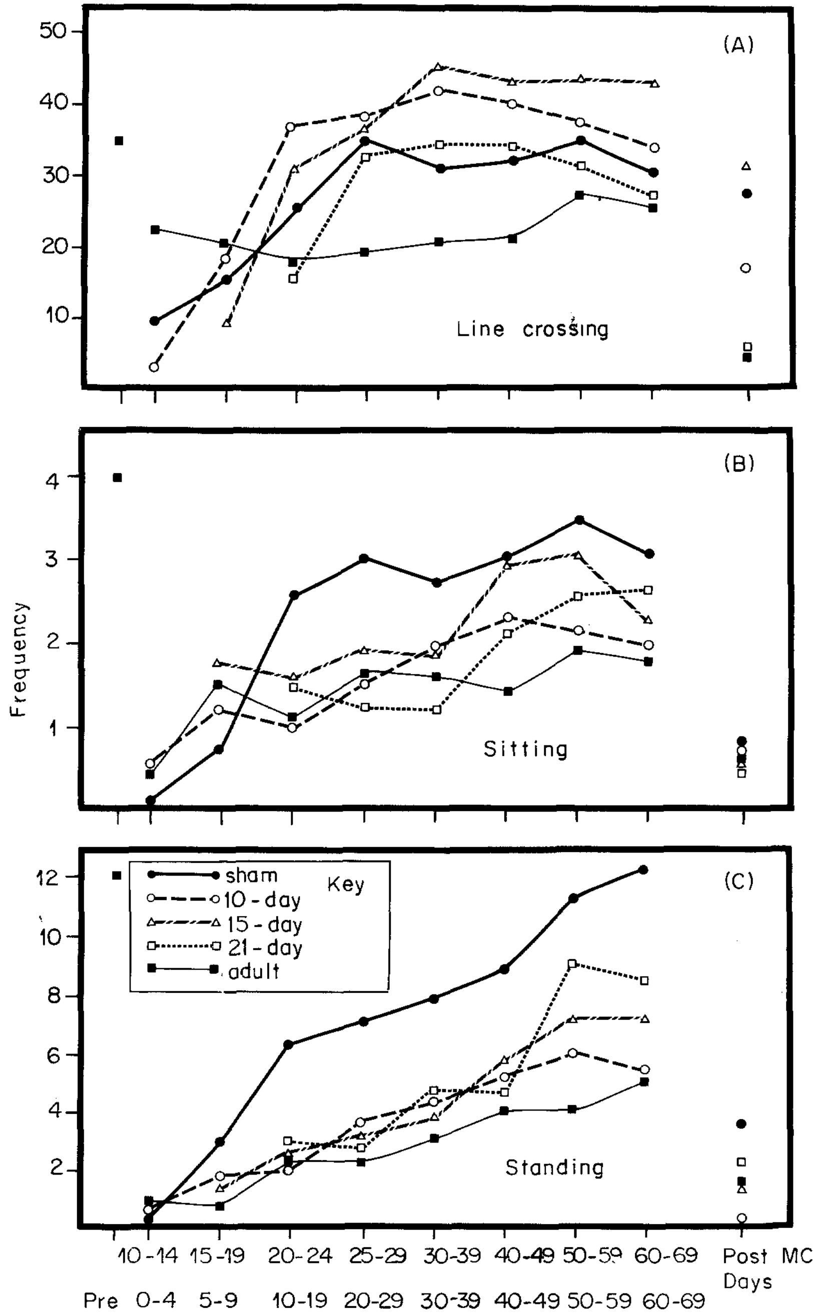
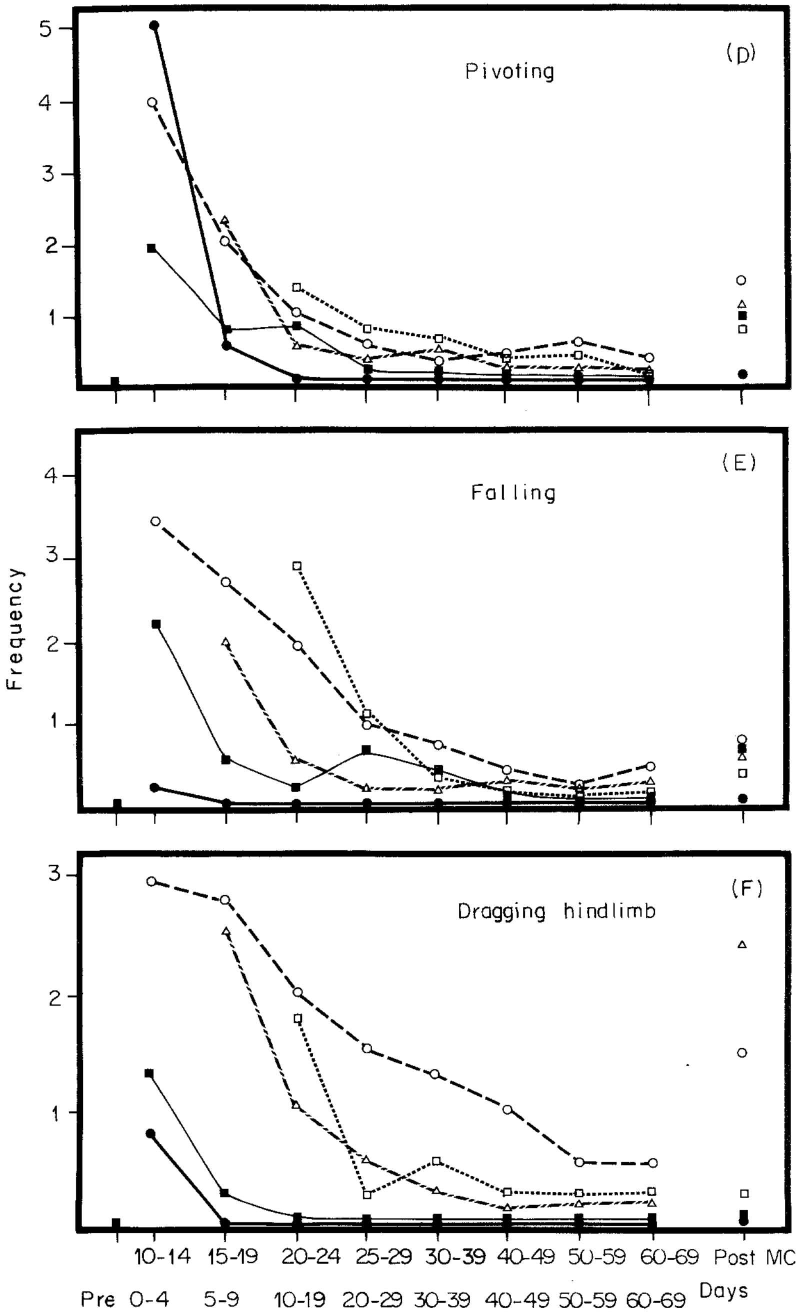


Fig. 2. Graphs of development of six open field activity measures following cerebellar lesions at four ages. A–line crossing; B–sitting without aid; C–standing, with or without



aid; D–pivoting; E–falling during locomotion or at rest; F–dragging a hind limb during locomotion. Higher labelling on abscissa for young-lesioned groups, in days of age; lower labelling on abscissa for adults only, in days following cerebellar lesion.

in the development of spontaneous activity (Fig. 2A). However, the frequency of sitting (Fig. 2B) and standing (Fig. 2C) both increased with age more slowly in all lesioned groups. Sitting reached control levels by 60 days ($P > 0.05$), while standing remained significantly lower in frequency for all experimentals ($P < 0.05$).

Three characteristics of infantile locomotion include falling, dragging a hindlimb, and pivoting (hindlimbs remain stationary as forelimbs pivot body around). Pivoting was common in the normal rats until 15-19 days of age; however, this behavior continued longer in the lesioned animals. All rats, except those lesioned at 10 days, were not significantly different from controls in this respect by age 25-29 days ($P > 0.05$) (Fig. 2D). Falling during locomotion occurred to a small degree in normal rat pups between ages 10-14 (Fig. 2E). During this same period, 10-day lesioned rats exhibited a high frequency of falling, which disappeared only slowly; the 15-day and 21-day groups were less affected on this measure. Differences from control in all groups were not significant ($P > 0.05$) after age 25-29 days. Dragging a hindlimb during locomotion was present in the 10-14 day normal rat pups, but this dropped to zero by the next test period (Fig. 2F). This behavior appeared more frequently and disappeared more slowly in all lesioned groups. However, unlike the two older groups, which approximated control levels within 15 days post-lesion, the 10-day group showed persistent and significant ($P < 0.05$) limb dragging until 50 days of age.

In normal rats, the total time spent on the suspended rope increased until 20 days of age, after which there was a rather sharp decline, as animals clung to the rope for shorter times before descending, and as they began to descend more rapidly (Fig. 3A). All experimental groups showed a similar biphasic curve, but the time did not decrease as rapidly with age as in normals; none of the lesioned rats scored at control levels until age 60-69 days ($P < 0.05$), or 30 days past the asymptote for the controls. However, when measured for actual times to descend (once descent was begun), none of the experimentals differed significantly from the controls at any age period ($P > 0.05$) (Fig. 3B). Thus, most of the difference in total time spent on the rope appears to be due to trials on which experimental animals did not descend at all during the 60 sec test. This is confirmed by data presented in Fig. 3C, the percent of all animals which descended the rope. Almost all normal rats descended within 60 sec by age 25-29 days. Experimentals took much longer to approach this level; by age 60-69 days, 10-day and 15-day lesioned groups descended on 90% of trials, while the 21-day animals descended 95% of the time. The percent of trials in which animals fell off the rope before 60 seconds decreased rapidly with age in all groups. Ten-day animals continued to fall on a small ($P > 0.05$ compared to controls), but consistent percent of trials even at 60-69 days of age (Fig. 3D).

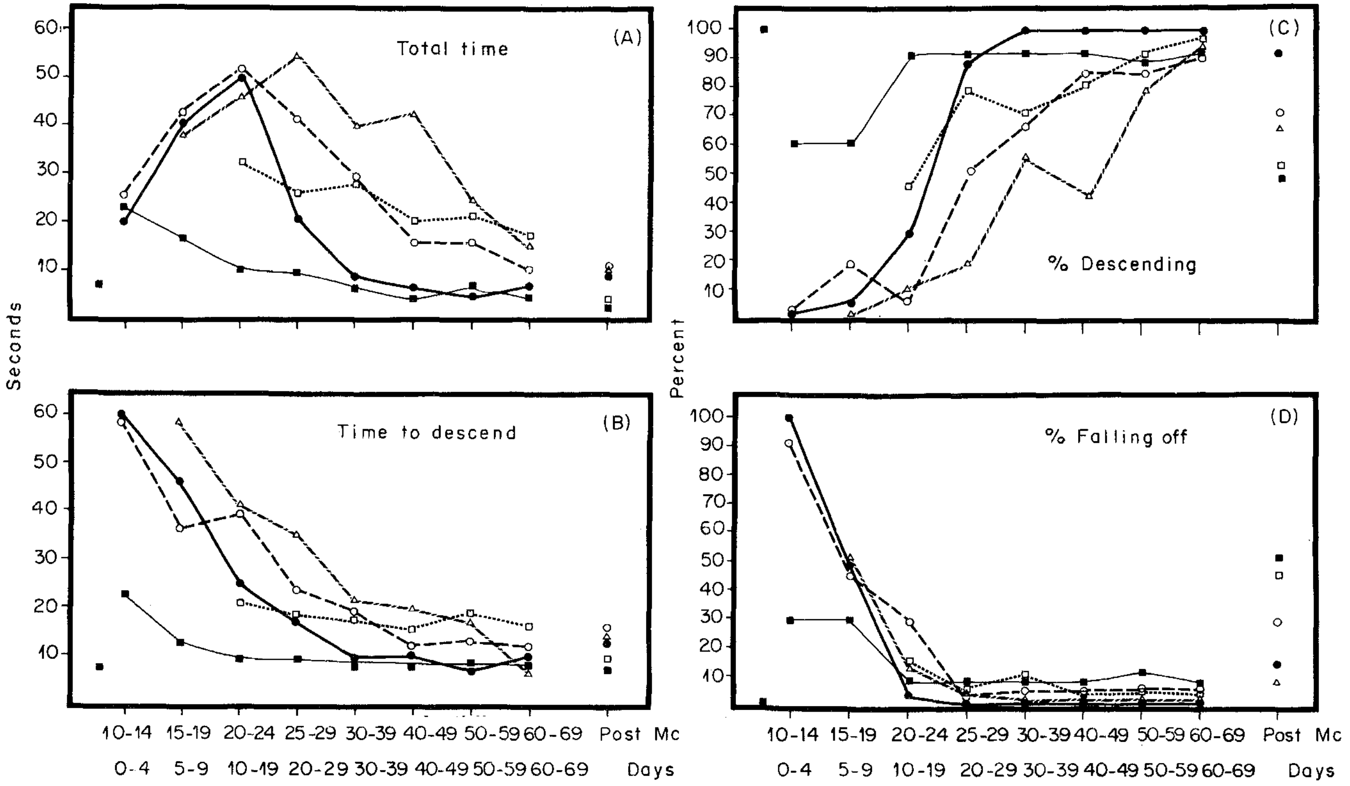


Fig. 3. Four measures on suspended rope; A—total time on rope; B—time to descend; C—percent descending; D—percent falling off. Symbols as in Fig. 2.

Total time spent on the narrow beam revealed a biphasic curve similar to that observed for time on the rope; that is, times increased between 10-19 days of age, then rapidly decreased to a low baseline as animals crossed the beam quickly without falling off. The experimental curves were less consistent, but in general revealed longer times spent on the beam throughout all age groups compared to controls (Fig. 4A). Again, the time taken to cross the beam was similar in all groups, but relatively higher in the experimentals (Fig. 4B) (at 60-69 days, $P < 0.05$ for 10-day and 15-day groups; $P > 0.05$ for 21-day group). The additional difference between experimental and normal groups in total time on the beam is explained by the data in Fig. 4C, percent crossing the beam. By age 20-24 days, normals crossed the beam on 100% of all trials. All experimentals asymptoted at around 65% crossing by age 25-29 days and remained at that level throughout testing. Normal rats fell off the beam frequently at age 10-14 days, but by age 15-19 days this was eliminated. A similar, but generally later elimination of this behavior occurred in the operates; however, animals of the 10-day group fell off infrequently ($P < 0.05$) but consistently, throughout testing.

Thus, on both rope and beam tests, those animals which did descend or cross, respectively, did so at rates comparable to controls. In addition, the increased times spent during trials by experimentals is represented for the most part by animals which clung to the rope or beam without initiating the "appropriate" behavior in the allowed time.

The results of the 60-69 day test in the alley are presented in Table 1. Controls contacted either side less than 0.5 times, average, per trial. All of the experimental groups scored significantly above the controls: The 21-day group scored 1.22 ($t = 2.19$, $P < 0.05$); the 15-day group scored 2.00 ($t = 3.45$; $P < 0.01$); the 10-day group scored 1.51 ($t = 2.80$; $P < 0.02$). However, none of the experimentals differed significantly from any other ($P > 0.05$).

EXPERIMENT 2

Methods

Six additional male Sprague-Dawley rats, weighing 250-300 g at the time of surgery, were used in this portion of the study. Animals were tested prior to surgery on all behavioral measures described in Expt 1. Following this initial test, animals were anesthetized with 50 mg/kg Nembutal, and the right half of their cerebella aspirated with a fine glass pipette. The cavities were filled with Gelfoam moistened with benzalkonium chloride.

Testing recommended 3 days after cerebellar surgery and continued approximately every 5 days until 20 days post-lesion, and thereafter every 10 days until the sixtieth post-operative day. Statistical comparisons were the same as in Expt 1. Histological procedures are described in Expt 3.

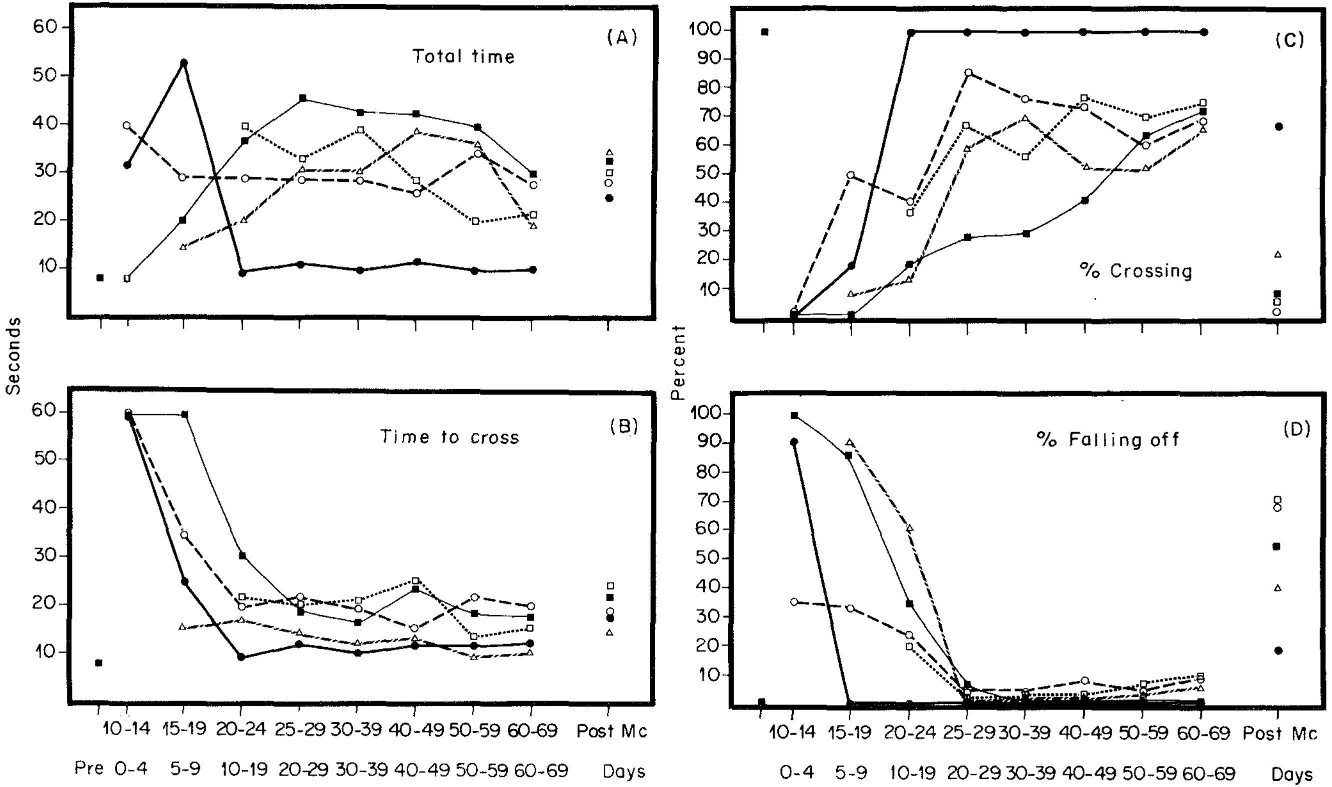


Fig. 4. Four measures on elevated beam: A–total time on beam; B–time to cross; C–percent crossing; D–percent falling off. Symbols as in Fig. 2.

TABLE 1

Alley Contacts Before and After Secondary Motor Cortex Ablation[a]

Group	Score at age 60-69 days (pre-motor cortex lesion)	Score at 5 days post-motor cortex lesion
10-Day cerebellar	1.51 ± 0.26	3.00 ± 0.44
15-Day cerebellar	2.00 ± 0.46	4.39 ± 0.67
21-Day cerebellar	1.22 ± 0.30	3.72 ± 0.77
Adult cerebellar	1.47 ± 0.50	2.50 ± 0.32
Control (no cerebellar damage)	0.39 ± 0.06	0.28 ± 0.16

[a] Scores represent the mean plus or minus the standard error of the mean.

Results

Histological analysis revealed that all animals received complete hemicerebellectomies with no brainstem damage. Lesions were comparable in size and extent to those of Expt 1. Coronal drawings representing minimal and maximal damage at three levels of the cerebellum are included in Fig. 1.

Spontaneous activity, as measured by line crossings in the open field activity box, was slightly reduced ($P < 0.01$) in the adults following cerebellar ablation (Fig. 2A). This lower activity rate persisted until nearly 50 days post-lesion, at which time scores began to increase back to preoperative levels. Sitting (Fig. 2B) and standing (Fig. 2C) were significantly reduced following the cerebellar ablation ($P < 0.001$); both increased toward preoperative frequencies very slowly over the 60 day test period. Pivoting appeared briefly following the lesion ($P < 0.01$); however, this recovered at least by the twentieth post-operative day ($P > 0.05$) (Fig. 2D). Falling increased well above normal on the first post-operative test period ($P < 0.01$); this frequency decreased rapidly, and was essentially absent by the 40th post-operative day ($P > 0.05$) (Fig. 2E). Dragging a hindlimb during locomotion, which appeared briefly following the cerebellar ablation ($P < 0.01$), recovered to normal levels ($P > 0.05$) by the 10-19 day period.

Total time spent on the suspended rope tripled immediately following cerebellar ablation (Fig. 3A). This increase was represented by a doubling of time to descend the rope ($P < 0.01$), which quickly recovered (Fig. 3B), and an increase in number of trials where animals did not descend within the allowed time. Percent descending dropped to 60% post-lesion, then returned to near normal ($P > 0.05$) within 10 days (Fig. 3C). Percent of animals falling off the rope during a trial increased to 30% over the pre-operative zero level; this also dropped quickly back to near normal ($P > 0.05$) within 10 days.

On tests involving the narrow beam, total time increased gradually over the first 30 days post-operative (Fig. 4A). This trend was not due to an increased time to cross, which actually decreased during this time period ($P < 0.01$) from an immediately post-operative high (Fig. 4B), but rather to an increase in the number of trials on which animals crossed (Fig. 4C) and to a decrease in the number falling off the beam (Fig. 4D).

Measurements in the automated alley (Fig. 5) revealed a very significant increase in the number of contacts immediately post-operative ($t = 12.78$, $P < .001$). These contacts decreased gradually with time following the lesions, and while they did not reach the low pre-operative level even by 60 post-operative days, the difference was not significant ($t = 2.41$; $P > 0.05$) after 40 days.

EXPERIMENT 3

Methods

All animals from Expt 1 and 2 were lesioned bilaterally in the motor cortex by aspiration, 60 days post-operative to the initial surgery. Following surgery, each animal received a single im injection of Duricillin.

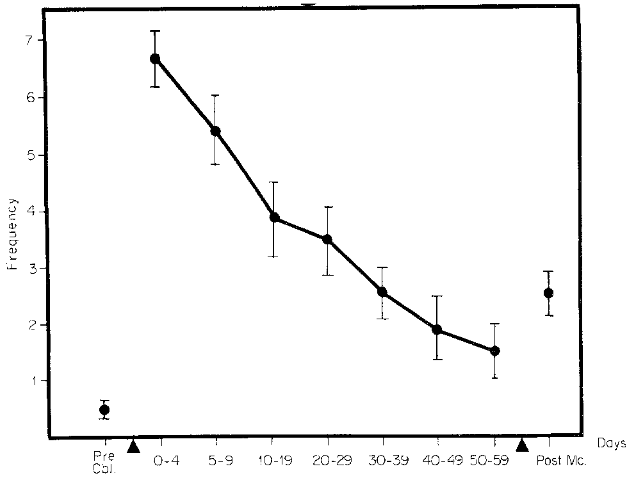


Fig. 5. Mean alley contacts over time following adult cerebellar and secondary motor cortical lesions.

Animals were tested on all of the behavioral measures described in Expt 1 five days after the secondary lesion of the motor cortex. Statistical comparisons were as in Expt 1 and 2.

Following the conclusion of testing, all animals were sacrificed with an overdose of Nembutal, then perfused through the heart with 10% formol saline. Brains were sectioned coronally on a freezing microtome at 50 μm, and representative sections through the cerebellar lesions stained with cresyl violet. Lesions were reconstructed, and sections examined microscopically to determine the extent of possible brainstem or contralateral cerebellar damage. Cortical lesions were plotted onto brain charts for comparison and analysis.

Results

The maximum and minimum extent of cortical damage for each group are represented in Fig. 6. Most of the lesions destroyed the entire dorsal surface of the anterior neocortex. Some dorsal medial somatosensory cortex was also ablated. None of the lesions invaded subcortical brain structures, except for variable damage to the corpus callosum. There was no apparent difference in lesion size or placement between the groups. In addition, there was no direct correlation of severity of motor symptoms with lesion size within each group.

Results of secondary motor cortex lesions on each behavioral measure are presented on the right margins of Figs. 2, 3, 4, and 5, and in Table 1. Five days following bilateral cortical ablation, spontaneous activity, sitting, and standing had decreased in all experimental ($P < 0.01$) groups. Line crossings (Fig. 2A) were most affected in the adult and 21-day groups ($P < 0.001$), while controls were not significantly affected ($P > 0.05$). Sitting (Fig. 2B) was equally depressed in all groups ($P < 0.01$). For standing (Fig. 2C), a graded reduction occurred in which the 10-day group was most affected, followed by the 15-day, 21-day, and adults, then controls; however, the differences between groups following cortical lesioning was not significant except between the 10-day group and controls ($P < 0.05$). Pivoting (Fig. 2D) was affected equally in all operates ($P < 0.05$), but not affected in controls ($P > 0.05$); falling (Fig. 2E) reappeared slightly but not significantly in all groups except controls (all, $P > 0.05$); dragging a hind limb during locomotion (Fig. 2F) returned only in the 10-day and 15-day operates ($P < 0.01$).

Total time spent on the suspended rope (Fig. 3A) was slightly depressed ($P < 0.05$) in all experimental groups, while time to descend (Fig. 3B) did not change. The overall percent of trials on which animals decended (Fig. 3C) decreased in controls to 85%, in 10-day and 15-day animals to about 70%,

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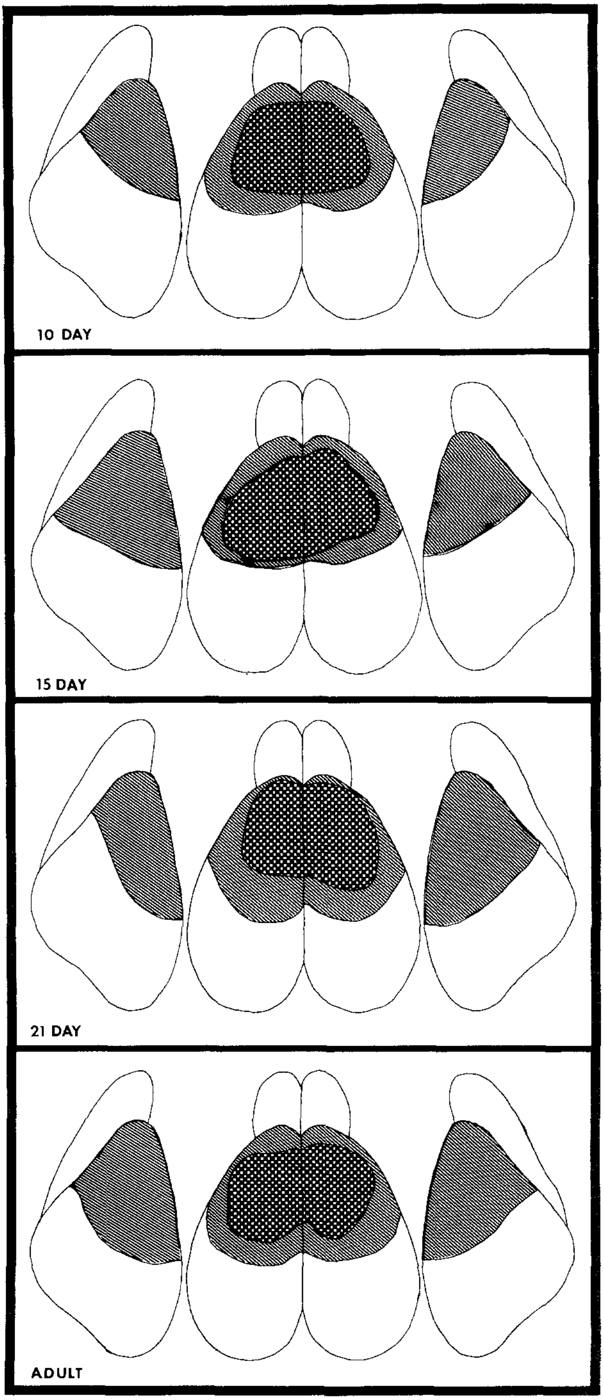
Fig. 6. Representations of minimal (checked) and maximal (striped) damage to neocortex in four groups of secondary lesions.


10 DAY
15 DAY
21 DAY
ADULT

and in 21-day and adult operates to about 50%. The percent falling off the rope (Fig. 3D) increased slightly ($P < 0.05$) in controls, to approximately 35% in the 10-day and 15-day groups ($P < 0.01$), and to approximately 50% in the 21-day and adult groups ($P < 0.01$).

Animals in none of the groups were affected by the secondary lesion ($P > .05$) on either total time on the narrow beam (Fig. 4A) or on time to cross the beam (Fig. 4B). However, the overall percent crossing (Fig. 4C) was significantly reduced in controls ($P < 0.02$), and drastically reduced in all operates ($P < 0.001$). Similarly, the percent falling off the beam (Fig. 4D) increased slightly in controls ($P < 0.05$), and greatly in all experimentals ($P < 0.01$).

Alley contacts measured 5 days following secondary lesioning are presented in Table 1. All animals except controls ($t = 0.59$; $P > 0.05$) and adults ($t = 1.98$; $P > 0.05$) showed a significant increase in contacts: 10-day animals scored 3.00 ($t = 3.65, P < 0.01$); 15-day animals scored 4.39 ($t = 3.29$; $P < 0.05$) and 21-day animals scored 3.72 ($t = 3.40; P < 0.02$).

DISCUSSION

The measurements of motor and postural development of normal rat pups in Expt 1 agrees well with data previously reported (Bolles and Woods, 1964; Gard, Hård, Larsson and Petersson, 1967; Altman, Anderson and Strop, 1971; Anderson and Altman, 1972). In addition, the maturational deficits caused by early cerebellar ablation appear similar to those induced by infantile cerebellar irradiation (e.g., Altman *et al.*, 1971).

The present study also suggests that cerebellar damage produces differential effects on motor development depending on the age at surgery. Spontaneous activity. as measured by line crossings in an open field situation, does not appear to be affected by cerebellar lesioning at any of the three ages. Frequency of sitting and standing, however, develops more slowly in all groups, particularly in the younger two. The developmental loss of the three "infantile" motor patterns, pivoting, falling, and dragging a hindlimb during locomotion, is also apparently slowed by cerebellar damage. On these latter measures the youngest-lesioned animals appear to be the most severely and permanently debilitated.

On most measures involving clinging to and descending the suspended rope the lesioned animals show maturational trends different from normal. Total time spent on the rope declined more slowly between age 25 and 69 days in operates, while actual time to descend was not significantly different at any age period. Operated animals descended the rope on fewer trials, especially between ages 25-69 days when normals descended 100% of the time. However, this does not appear to be due to more operates falling off at these ages, but rather to those who spent the entire test period clinging to the top of the rope.

All groups of operates spent more time on the narrow beam than did normals between ages 20 and 69 days. Part of this difference was due to a slower crossing time in all lesioned rats between ages 20 and 49 days, and in the youngest-lesioned animals thereafter. Percent of trials on which animals crossed the beam was significantly lower in experimentals than controls from age 20 days onward; all operates asymptoted at around 65% compared to 100% for the normals. Only the 10-day operates appeared to have a long-lasting deficit in their ability to balance on the beam at all. This was represented by a small percent of trials on which animals continued to fall off even at the 60-69 day age period.

It appears from this analysis that the older groups recovered more rapidly and more completely on nearly all measures than did the youngest-lesioned group. The animals of the 10-day group had some residual motor disabilities on nearly all tests even by the oldest test period when compared to controls. The only deficits recorded in the 15-day or 21-day groups at that time were in descending the rope and crossing the narrow beam. Thus, basic postural and locomotor patterns remained problems only to the youngest-lesioned groups, while more difficult patterns of coordinated behavior, such as turning around and descending on the rope, and balancing in a narrow space, were affected in all groups more permanently.

This finding appears contrary to most studies which compare recovery following brain damage in young and older animals. In general, behavioral deficits produced in infant operates attenuate more rapidly and completely than those in adults (see, e.g., Rosner, 1970). Pertinent to this apparent contradiction is a study by Hicks *et al.* (1969), in which rats with bilateral fastigial nuclear ablation in infancy were severely and permanently incapacitated, while the cerebellectomized adults showed some recovery in a period of weeks. In addition, Thompson, Harlow, Blomquist and Schiltz (1971) found that performance on delayed responding, and on other tasks related to the frontal cortex, was less disrupted when tested soon after surgery in the older animals compared to younger operates. Thus, there is some precedent for the present findings that the 21-day lesioned rats developed (recovered) a more normal motor behavior than did the 15-day and especially the 10-day lesioned animals.

In conjunction with the observed differences in rate and degree of development of normal motor and postural behavior in the three young-lesioned groups, the results of Expt 2 suggest that unilateral cerebellar damage in the adults produce longer lasting motor and postural deficits than in any of the younger operates. Thus, while the absolute comparisons of frequencies for standing, sitting, etc. in the open field situation may not be relevant due to the lower rate of spontaneous activity in the adults, it appears that on all open field behavioral measures, except dragging a hindlimb during locomotion, adults recovered over a much longer time course and to less completion than younger operates. Many of the measures on the suspended rope and the narrow beam also support this conclusion.

From the combined findings of Expt 1 and 2, it appears that rats at the very beginning of motor development (10-day group) and those in which motor development is completed (adult group) show the most persistent and debilitating effects of hemicerebellectomy. On some tests, the deficits in adults compared to 10-day operates were less severe but equally persistent after surgery.

It is interesting to note that following motor cortex lesions, very few behavioral measures were affected *only* in the secondarily-lesioned animals and not in those animals with cortical lesions alone. These measures include spontaneous activity, pivoting, falling and dragging a hindlimb during locomotion, and contacts with the alley during ambulation. Thus, while few studies to date have reported motor deficits following distruction of this area in rats (Maier, 1935; Zimmerman, Chambers and Liu, 1964; Castro, 1972; Van Hasselt, 1973) it appears that these animals are either slightly or severely defective on several motor tasks, especially those involving fine balance and coordination or initiation of motion.

In rats which had recovered from cerebellar damage, secondary lesions of the motor cortex reinstated many of the cerebellar symptoms in some animals. Most severely affected were the rats which received hemicerebellectomies at 10 days of age. Fifteen-day operates were nearly as debilitated on most measures, while 21-day operates and adults were least affected, either in relation to their own pre-cortical levels or to cortical controls.

This effect in the adults was contrary to reports in several other species in which secondary lesions of the motor cortex will reinstate much of the original cerebellar syndrome in recovered animals (see Smith *et al.*, 1974, for a discussion). Significantly, these secondary lesions in the present study produced dissimilar effects in the age groups used, emphasizing the probability that recovery in the younger- and adult-lesioned groups proceeds by different mechanisms. It may be that the neocortex has a greater potential for plasticity in the neonates, whether through the formation of new or altered synaptic contacts (Lynch, Smith and Cotman, in press), or through possible enzymatic or other regulation of remaining, normal pathways. This may also explain the suggested interspecies differences; animals with more highly developed neocortex may retain such "infantile" potential for plasticity into adulthood.

An alternate hypothesis may be that recovery proceeds through the "path of least resistance." Thus, in the adult rat the neocortex *may* have the potential to reorganize, thereby compensating for partial cerebellar damage, but other links in the output towards locomotor and postural behaviors may alter more rapidly or easily in response to the lesioned condition. As shown previously (Smith *et al.*, 1974), this may be accomplished to some degree by the remaining, contralateral cerebellum in the adult rat. Other possibilities as yet unexplored in this regard include the pathways involving the ventral lateral nucleus of the thalamus, the red nucleus, brainstem reticular formation, or lateral vestibular nuclei. Speculations regarding plasticity in these latter brain areas in response to cerebellar damage, and their potential role in recovery must await further physiological and biochemical analysis.

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