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Effects of Lesions of the Cerebellar Vermis on VMH Lesion-Induced Hyperdefensiveness, Spontaneous Mouse Killing, and Freezing in Rats[1]

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SUPPLE, W. F., JR., J. CRANNEY AND R. N. LEATON. *Effects of lesions of the cerebellar vermis on VMH lesion-induced hyperdefensiveness, spontaneous mouse killing, and freezing in rats.* PHYSIOL BEHAV **42**(2) 145–153, 1988.—In a series of independent experiments, we showed that lesions of the vermis of the cerebellum in rats blocked the hyperdefensiveness induced by lesions of the ventromedial hypothalamus (VMH), attenuated spontaneous mouse killing, and reduced unconditioned freezing and other signs of fear in the presence of a cat. The vermal lesions did not significantly affect foot-shock conditioned freezing. Control lesions of the cerebellar hemispheres did not affect VMH lesion-induced hyperdefensiveness or freezing in the presence of a cat. The hemispheric lesions did attenuate foot-shock conditioned freezing. The data are discussed in terms of the striking similarities and differences between the behavioral effects of cerebellar vermal lesions and amygdala lesions and the interaction of a number of brain areas in modulating agonistic behaviors. The results leave no doubt that the medial cerebellum is significantly involved in the control of species-specific agonistic behaviors. The specific dimension of agonistic behaviors and the details of the interactions with other brain areas remain a puzzle which we approached here by expanding the behavioral profile of animals with lesions of the cerebellar vermis.

Cerebellum Vermis Cerebellar hemispheres VMH Defensive behavior Agonistic behavior Mouse killing Freezing Species-specific behavior Cat Foot shock

IT has become increasingly clear that the cerebellum is involved in a variety of behaviors that go well beyond its classical role in the coordination of motor activity [35]. The medial cerebellum—the vermal cortex and associated fastigial nuclei—has been implicated in the control of a variety of complex motivational and emotional behaviors [9, 15, 20, 32], and these cerebellar areas have rich anatomical connections with limbic and hypothalamic areas long associated with motivation and emotion [13, 21, 30]. Increased "pleasure reactions" in cats and marked "taming" in monkeys were reported following lesions of the cerebellar vermis [6, 12, 29]. In rats, lesions of the fastigial nuclei attenuated the hyperemotionality produced by septal lesions [8]; and we recently showed that lesions of the cerebellar vermis attenuated a variety of fear-related or defensive behaviors in rats [32]. In the present experiments, we have attempted to extend the behavioral profile of the cerebellum in defensive and agonistic behaviors. Specifically, in separate experiments we examined the effects of lesions of the cerebellar vermis or the cerebellar hemispheres on (1) hyperdefensive behavior induced by lesions of the ventromedial hypothalamus (VMH), (2) spontaneous mouse killing, and (3) freezing to foot shock or to a cat stimulus.

EXPERIMENT 1

Lesions of the VMH provoke hyperreactivity or hyperemotionality in a number of mammalian species, including humans [3]. These reactivity changes were originally interpreted as increased savageness or aggressiveness [24,36], but more recently they have been interpreted as heightened defensiveness [2,3]. VMH hyperdefensiveness has proved to be very persistant, in most cases lasting as long as the animal lives, and very resistant to environmental manipulations or selective brain damage [3,4]. Amygdala lesions, which alone can reduce defensive behavior [3], were without effect in attenuating the "savage" behavior of VMH-lesioned cats [24]. Lesions of the mesencephalic cen-

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tral gray produced only a temporary loss of "VMH savageness" [18], and large lesions of the lateral tegmentum abolished "savageness" but left the cats almost completely unresponsive to external stimuli [22]. Relatively small lesions of the lateral tegmentum were reported to permanently abolish "savageness" without producing grossly observable behavioral impairment [18]. Less attention has been devoted to attempts at altering VMH hyperdefensiveness with additional brain damage in rats, but two brief reports indicated that the syndrome was attenuated by lesions of the amygdala [27,34]. Neither report provided procedural or anatomical detail, and one [27] differed from most other reports by finding VMH hyperdefensiveness to be quite temporary.

Similar reactivity changes are produced by lesions of the lateral septal area, but the "septal syndrome" is consistently found to be relatively temporary, and it is readily attenuated by additional brain damage, particularly by lesions of the amygdala (see [3] for review). Berntson and Torello [8] showed that lesions of the cerebellar fastigial nuclei attenuated the hyperdefensiveness induced by septal lesions. The relative permanence and resistance to change of the hyperreactivity induced by VMH lesions, and the interpretation of the hyperreactivity as hyperdefensiveness, make it a useful substrate against which to evaluate the changes in defensive behaviors produced by medial cerebellar damage [6, 7, 9, 29, 32]. In Experiment 1, we evaluated the effects of lesions of the cerebellar vermis on the reactivity changes induced by VMH lesions. The vermal effects were compared with effects produced by bilateral lesions of the cerebellar hemispheres to provide a control for any general debilitating effects of the cerebellar damage.

METHOD

Subjects, Surgery and Histology

Thirty-four male Sprague-Dawley derived rats, 70–100 days old at the time of surgery were used. They were individually housed with ad-lib access to food and water throughout the experiments. Testing occurred during the light portion of a 14:10 hr light-dark cycle. The rats were randomly assigned to one of four lesion groups. One group (n=8) received bilateral lesions of the ventromedial nuclei of the hypothalamus (VMH); one (n=8) received lesions of the cerebellar vermis (VER); one (n=12) received bilateral VMH lesions and cerebellar vermal lesions in one stage (VMH+VER); and one (n=6) received bilateral VMH lesions and bilateral lesions of the cerebellar hemispheres in one stage (VMH+HEM).

All surgery was performed using clean but not aseptic conditions with the aid of a headholder that did not require the use of ear bars [17]. Rats were anesthetized with sodium pentobarbital (45 mg/kg) following pretreatment with atropine sulphate (20 mg/kg). For the VMH lesions electrodes were stereotaxially oriented according to the atlas of Pellegrino, Pellegrino and Cushman [28] to the following coordinates: AP=0.0 referenced to bregma, L=±1.0, V=9.3 below the dural surface. Lesions were made electrolytically with a 2-mA anodal current for a duration of 15 sec. Electrodes were constructed of 27-ga stainless steel hypodermic tubing insulated except for .5 mm at the tip. The cerebellar lesions were made by aspiration and were visually guided with the aid of a dissecting microscope. Access to the vermis was achieved by removing a 4×5 mm section of the interparietal bone overlying the midline of the cerebellum. For the hemispheric aspirations, this center bone strip was spared and the lateral parts of the interparietal bone were removed bilaterally. The space created by the aspirations was loosely packed with Gelfoam before the wound was closed.

Following testing the rats were given an overdose of sodium pentobarbital and perfused intracardially with normal saline followed by 10% buffered formalin. The brains were hardened further in formalin and embedded in gelatin. Frozen sections (20 microns) were made through the extent of the lesions, and every tenth section was mounted and stained using a modified Kluver-Barrerea technique. The lesions were reconstructed by projecting the images of the sections onto atlas plates from [28].

Procedure

Ratings of each rat's behavioral reactivity were made by trained observers on the three consecutive days before surgery and on seven consecutive days beginning with the day following surgery. The reactivity ratings, modified from those described by Brady and Nauta [11], consisted of three sub-scales. Scale I determined the rat's reaction to the eraser end of a pencil presented directly in front of and 3 cm away from its snout. Ratings were 0=no response; 1=orientation; 2=single bite; 3=repeated biting. Scale II assessed the rat's reaction to gentle prodding of the dorsum with the eraser end of a pencil. Ratings were 0=no response; 1=orientation; 2=flinch or vocalization; 3=jumping or escape attempt. Scale III assessed resistance to capture and handling. An attempt was made to pick up the rat around the shoulders using a gloved hand. Ratings were 0=no response; 1=vocalization or avoidance; 2=struggling; 3=struggling with biting. Responsiveness on Scales I and II was assessed 10 times per day with a 5 sec interval between tests. Responsiveness on Scale III was assessed 5 times per day with approximately 10-sec intervals between tests. A total reactivity score for each rat for each day was taken as the mean of the three sub-scale scores. All ratings were conducted in the rat's home cage and without knowledge of group membership. The rats were not systematically handled prior to the experiment.

RESULTS

Histology

Figure 1 shows a representative lesion of each type. There were no apparent differences in the extent of the specific lesion types among the different lesion groups. The VMH lesions, shown on the left of the figure, were quite large, extending approximately 2 mm posteriorly beginning at the medial aspect of the anterior hypothalamic area. There was slight bilateral damage to the lateral hypothalamic area, the arcuate nuclei and the ventral surfaces of the dorsomedial nuclei. Damage to other surrounding structures was typically slight and unilateral. The extent of the vermal lesions is shown in the middle portion of the figure. Anterior to the primary fissure these lesions extensively damaged the dorsal portion of the central lobule (lobule III following the terminology of Larsell [25]) and virtually completely destroyed the ventral (IV) and dorsal (V) lobules of the culmen. Posterior to the primary fissure the declive (VI) and tuber vermis (VII) were destroyed and the pyramid (VIII) was extensively damaged. Damage did not extend into the uvula (IX). The lesions extended ventrally into the white matter, but the cerebellar nuclei were not damaged. The lesions to the cerebellar hemispheres, shown on the right of the figure, were essentially bilaterally symmetrical and did not

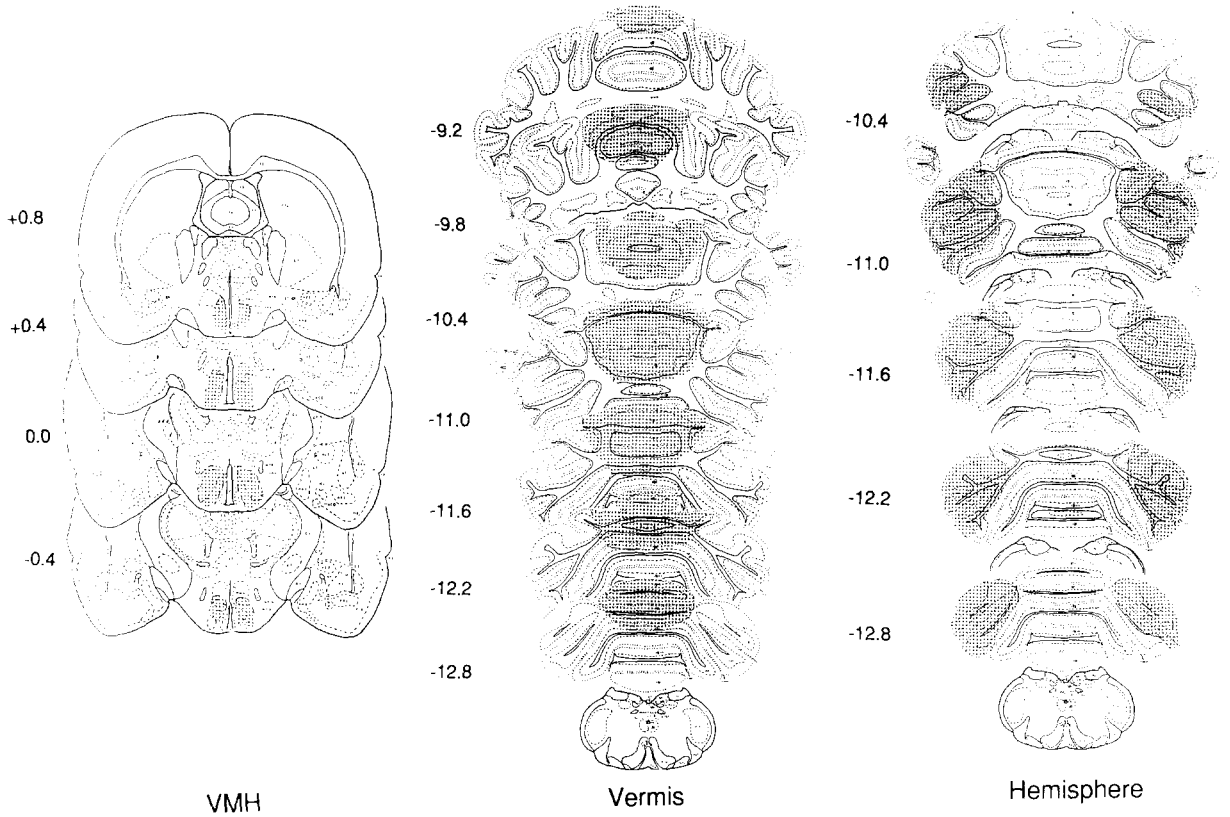

FIG. 1. The shaded areas show the extent of a representative VMH, Vermis and Hemisphere lesion superimposed on frontal sections from Pellegrino, Pellegrino and Cushman [28]. Coordinates shown are mm referenced to bregma.

encroach upon the midline cerebellar areas involved in the vermal lesions. These lesions extended anteriorly to the posterior portion of the simplex lobule which was slightly damaged. Posteriorly the anterior portions of the paramedian lobule were extensively damaged. Otherwise, the damage was confined primarily to Crus I and Crus II, which were virtually completely destroyed. Damage did not extend into the paraflocculus. The underlying white matter was invaded, but the cerebellar nuclei were not damaged.

Behavioral Reactivity

Figure 2 shows the total reactivity ratings for the three pre-operative and seven post-operative days. Repeated measures analysis of variance for the pre-operative days revealed no significant group differences, $F<1$. The reduction in reactivity over pre-operative days was significant, $F(2,60)=13.18$, $p<0.001$, but the interaction did not approach significance, $F<1$. For the post-operative days the group differences in reactivity were significant, $F(3,30)=22.67$, $p<0.001$. Newman-Keuls post-hoc comparisons of the overall post-operative ratings showed that the VMH and VMH+HEM groups did not differ significantly, $ps>0.05$, but both of these groups were significantly more reactive than either the VMH+VER group or the VER group, $ps<0.05$. The VER and VMH+VER groups were not significantly different, $p>0.05$. The change in reactivity over the post-operative days was significant, $F(6,180)=3.85$, $p<0.01$. Within group analyses compared the change in reactivity scores from the three pre-operative days to the seven post-operative days. The increase in reactivity was statistically significant for the VMH group, $t(7)=10.55$, $p<0.001$, and for the VMH+HEM group, $t(5)=5.37$, $p<0.01$. The reactivity change was not significant for the VMH+VER group, $t<1$, but the slight decrease in reactivity shown by the VER group was marginally significant, $t(7)=2.29$, $p=0.055$. The same pattern of differences was shown by all groups in the scores for the three sub-scales that contributed to the total reactivity score.

DISCUSSION

The lesions of the cerebellar vermis prevented the appearance of the hyperdefensive behavior characteristic of rats with VMH lesions. Rats that received lesions of the VMH alone showed the expected increase in reactivity following surgery while the animals that received both a VMH lesion and a lesion of the cerebellar vermis showed no post-operative change in reactivity. Bilateral lesions of the cerebellar hemispheres in combination with the VMH lesions were ineffective in altering the VMH lesion-induced behavioral changes.

These data are consistent with several reports which suggest that defensive behaviors are attenuated by lesions of the cerebellar vermis or associated fastigial nuclei [6, 7, 9, 29, 32]. The hyperreactivity of the VMH-lesioned animal provided an effective baseline against which to evaluate changes induced by vermal lesions. Although no significant effect on reactivity was found with the vermal lesion alone, this group did show a slight post-operative decrease in reactivity, and a floor effect may well have prevented detecting

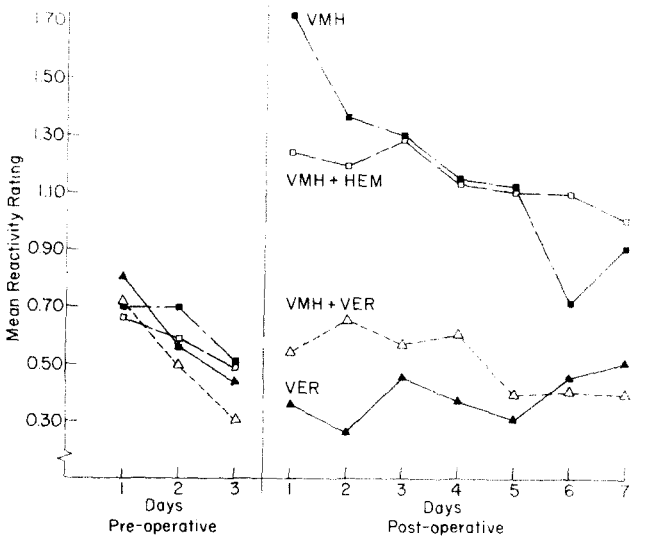

FIG. 2. Mean total reactivity rating for the three pre-operative and seven post-operative days for the four groups in Experiment 1.

any changes. The present data parallel particularly well the report of Berntson and Torello [8] that fastigial nuclear lesions attenuated the hyperreactivity induced by septal lesions in rats. In that report, the effects of the septal lesion alone had disappeared within the first four post-operative days, and the effects of the combined fastigial lesions were not detectable beyond that point. In the present experiment, the VMH lesions induced a persistent reactivity change against which to evaluate the attenuating effects of cerebellar damage. Although the VMH-induced reactivity differences did diminish over the post-operative test days, the differences in reactivity were still significant on the seventh post-operative day, $F(3,30)=3.11$, $p<0.05$.

It has been a common working hypothesis that the medial hypothalamus plays a central role in the suppression of reactivity and that VMH hyperreactivity is a release phenomenon (see, for example [1]). The "taming" effects often seen following amygdala lesions are assumed to be mediated through the medial hypothalamus. This assumption is based in large part on the well established result in cats that VMH hyperreactivity is not altered by prior or subsequent amygdala lesions [24]. However, the picture for the rat is not as clear. There are only two rather unsatisfactory reports of the effects on reactivity of combined amygdala and VMH lesions in rats [27,34]. The answer to whether or not this represents a true species difference in the neural control of reactivity awaits further research. However, it is clear from the present data that the attenuation of defensive behavior associated with cerebellar vermal lesions does not depend upon the VMH in the rat. It seems reasonable to assume as a working hypothesis, based upon the available evidence in the rat, that the amygdala, medial hypothalamus, septal area, and medial cerebellum converge on some other brain area, possibly in the mesencephalon (see [1]), to modulate an animal's reactivity along many dimensions. Anatomical or physiological data have shown relatively direct, and possibly reciprocal, connections between the medial cerebellum and all of these brain areas [13, 19, 21, 30].

In any study involving damage to the cerebellum, the issue of motor impairment is critical, both general, nonspecific impairments and more subtle motor dysfunctions. Two facts make it unlikely that the effects of cerebellar vermal lesions on defensive behavior were related to nonspecific impairments. First, although both the vermal and the hemispheric lesions produced mild ataxia and tremor in many rats, the condition had cleared completely by the third post-operative day. If the first three days were excluded from the post-operative statistical analyses the group difference remained significant, $F(3,30)=13.67$, $p<0.001$, and the post-hoc comparisons yielded the identical pattern of group differences, $ps<0.05$, as did the analysis of all 7 post-operative days. Second, the lesions of the cerebellar hemispheres, which might be expected to produce as severe a general impairment as the vermal lesions, had no detectable effect on the reactivity changes induced by the VMH lesions. Of course, the question of subtle, but significant, motor dysfunctions remains and can only be answered by viewing a consistent pattern of results over many different experimental paradigms.

EXPERIMENT 2

As discussed above, either septal lesions or VMH lesions induce hyperdefensivness in rats. Amygdala lesions induce docility, attenuate septal lesion-induced hyperdefensiveness, and perhaps attenuate VMH lesion-induced hyperdefensiveness as well (see [2]). Lesions of the medial cerebellum, like amygdala lesions, produce docility [6,29], attenuate septal lesion-induced hyperdefensiveness [8], and as we showed in Experiment 1, attenuate VMH lesion-induced hyperdefensiveness. Septal area, VMH and amygdala interact in similar ways in the modulation of other forms of agonistic behavior. Either septal lesions or VMH lesions induce species-specific mouse killing in rats. Amygdala lesions can block mouse killing in rats that spontaneously kill mice and in rats induced to kill by septal and VMH lesions (see [2]). Guided by the ineractions of the medial cerebellum with septal and VMH hyperdefensiveness, and the general similarities of the effects produced by amygdala and medial cerebellar lesions, the present experiment studied the effects of cerebellar vermal lesions on spontaneous mouse killing in rats.

METHOD

Subjects, Surgery and Histology

Forty male albino rats (Holtzman) were 90–100 days old at the time of surgery. They were individually housed and allowed ad lib access to food and water. Surgical and histological procedures were the same as those described in Experiment 1. Twenty randomly selected rats received aspiration lesions of the cerebellar vermis. Twenty sham-operated controls were treated identically except the skulls were not opened. Prior to the present experiment all rats were tested for acoustic startle response and in several defensive behavior paradigms [32]. Testing for mouse killing began a minimum of 14 weeks following surgery. One of the sham-operated rats died before testing.

Procedure

All tests were conducted in the rat's home cage during the light portion of the 14:10 hr light-dark cycle. An adult male albino mouse was introduced to the rat's cage, and the rat's immediate response to the mouse was recorded. The cages were then checked after intervals of 5, 30, 60, and 120 min and then after 24 hr. Dead mice were removed from the cages when found.

RESULTS AND DISCUSSION

The vermal lesions were similar to those described in Experiment 1 and summarized in Fig. 1. The lesions are fully described in [32].

Six of the 19 sham-operated rats (31.6%) killed the presented mouse. Only 1 of the 20 vermal lesioned rats killed (5%). Analysis of these kill frequencies yielded a chi-square value of 4.68, $p<0.03$. Of the 6 killers in the sham-operated group, 5 killed within the first min of exposure to the mouse and the sixth had killed by the 5 min mark. The 1 killer in the vermal lesioned group did not kill immediately but did kill within the first 5 min. No killing occurred in either group after the 5 min mark.

Once more we found results indicating the involvement of the cerebellar vermis in the modulation of agonistic behaviors. The effects of vermal lesions again were similar to the reported effects of amygdala lesions, which produce long-lasting attenuation of mouse killing [23]. Animals with amygdala lesions eventually recover their preoperative mouse-killing behavior, and amygdala lesions may facilitate the development of killing under some conditions [23]. We cannot determine from the present data whether the similarities of the effects of cerebellar vermal lesions and amygdala lesions on mouse-killing behavior extend to these complexities associated with amygdala lesions.

A general, non-specific motor impariment could have played a role in suppressing mouse killing, but the nature of the killing response suggests otherwise. A rat either kills or does not kill, and when it does kill it does so quickly. There is rarely a pattern of abortive kills, a mouse attacked but not killed. This pattern held in the present experiment. The non-killers in either group simply left the mouse alone. There were not attacks or killing attempts which were aborted because of apparent motor defects. In addition, the animals were tested 14 weeks following surgery (as compared to the immediate post-surgery tests in Experiment 1), and there were no obvious motor deficits at that time. We cannot rule out the influence of more subtle motor dysfunctions, particularly in the absence of a lesion control group, but a specific effect on agonistic behavior provides a better fit for the overall pattern of results emerging for rats with lesions of the cerebellar vermis.

EXPERIMENT 3

We previously reported [32] that lesions of the cerebellar vermis reduced a variety of fear-related behaviors in rats. In that report freezing behavior produced a rather puzzling outcome. Rats with vermal lesions froze less in the presence of a cat, a result consistent with the other indices of reduced fear. But surprisingly, the vermal-lesioned rats did not differ from controls in freezing to foot shock. This result was difficult to reconcile with a general fear-reduction interpretation of vermal lesions, and it represented a striking exception to the parallels between the behavioral effects of vermal and amygdala lesions. The amygdala reduces freezing to both foot shock and cats [10].

Experiment 3 was an attempt to replicate our previous results with cerebellar vermal lesions and freezing to cats and foot shock. Lesions of the cerebellar hemispheres provided an operated control group not present in the previous study.

METHOD

Subjects, Surgery and Histology

Thirty-six male Long-Evans derived rats were 90–110 days old at the time of surgery. Surgical and histological procedures were the same as those described in Experiment 1. Twelve randomly selected rats received aspiration lesions of the cerebellar vermis, twelve received bilateral aspiration lesions of the cerebellar hemispheres, and twelve served as sham-operated controls. Testing began a minimum of 6 weeks following surgery. Prior to this experiment, all rats were tested for acoustic startle response.

Apparatus and Procedure: Shock

Conditions were basically identical to those described previously [32]. The apparatus consisted of two identical 23.5×29×19.5 cm observation chambers. The long walls were stainless steel while the others were clear acrylic. The grid floor was composed of 2.5-mm stainless steel rods spaced 1.25 cm apart and wired to a Grason-Stadler shock generator and scrambler. The chambers were housed within sound attenuating chambers that had 30×30 cm observation windows. Illumination was provided by a 7.5-W white light bulb mounted in the center of the larger chamber's ceiling. Ventilation fans produced 72-dB noise which helped mask extraneous sound.

Rats were placed singly in an observation chamber and after 1 min received a single, 1 mA scrambled foot shock of 0.75 sec duration. The rat's behavior was rated with a time-sampling procedure every 4 sec for the min prior to shock and for 5 min immediately following shock. Behavior was scored as belonging to one of the following 5 categories: (a) freezing: complete body immobility, including vibrisse, but excluding the movements required for respiration, (b) active: non-specific generalized activity occurring anywhere within the chamber, (c) rearing, (d) grooming and (e) other. Forty-eight hours after training, each rat was returned to the chamber and behavior was rated for one 5 min test in extinction. Following each session the number of fecal boli was recorded and the chamber was cleaned with a 5% ammonium hydroxide solution.

Apparatus and Procedure: Cat

Testing occurred in a 125×75×70 cm arena with walls, floor, and ceiling constructed of clear acrylic. Centered within this arena was a 30×30×30 cm clear acrylic chamber with a grid floor. Illumination was provided by a shielded 60-W white light bulb centered 125 cm above the arena.

Testing began approximately 3 weeks after completion of the shock tests. Each rat was placed individually into the smaller chamber and the lid was fastened to prevent the cat from contacting the rat. After 1 min the cat, a 4-kg, 2-year old female, was introduced to the outer arena. The dimensions of the arena permitted the cat to move freely about the apparatus. The rat's behavior was rated every 4 sec for the min before the introduction of the cat and for 8 min after the cat was introduced. Behavior was rated according to the previously described categories. Following each session the number of fecal boli was recorded and the arena was cleaned.

All ratings were done without knowledge of group membership. These procedures have yielded inter-observer correlations ranging from .95 to .98.

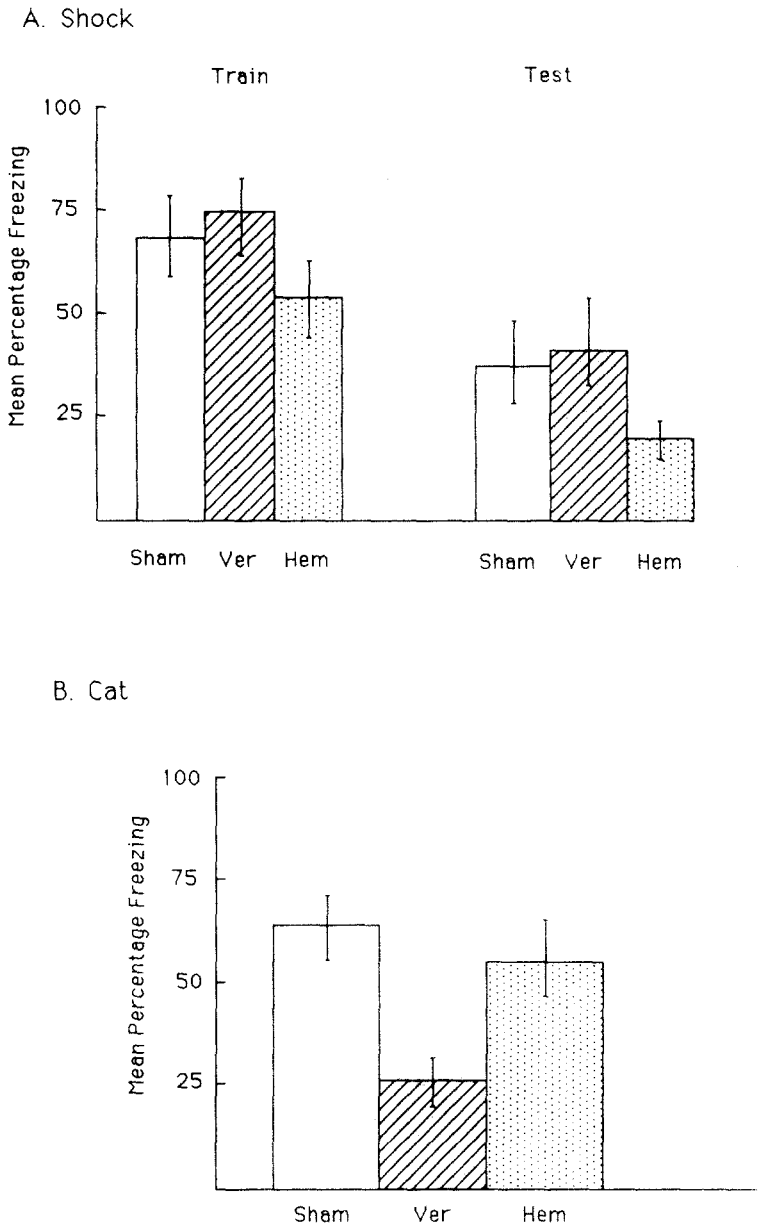

FIG. 3. Mean percentage (±SEM) of behavioral samples scored as freezing for the three groups in Experiment 3. (A) Percentage freezing for the 5 min immediately following a single, 1-mA foot shock (Training) and for the 5 min extinction session run 48 hr later (Test). (B) Percentage freezing during the 8 min exposure to the cat.

RESULTS

The lesions were similar to those described in Experiment 1 and summarized in Fig. 1.

Shock Test

Figure 3A shows the mean percentage of freezing in the shock training and test sessions. Although the hemispheric-lesioned group appeared to freeze less during training analysis of the training session yielded only a marginally significant effect, $F(2,33)=2.67$, $p<0.09$. However, analysis of the test session showed a significant difference among the groups, $F(2,33)=5.75$, $p<0.01$. Newman-Keuls post-hoc comparisons of this difference showed that the hemispheric-lesioned group froze significantly less than either of the other two groups, $p<0.05$. The only other behavioral sample to yield a significant group difference was rearing which was significant for both training, $F(2,33)=5.20$, $p<0.01$, and testing, $F(2,33)=7.14$, $p<0.01$. For both sessions, the hemispheric-lesioned group reared significantly more than either of the other two groups, $ps<0.05$. The vermal-lesioned group and the sham-operated group did not differ significantly on any measure during shock training or testing. There were no significant group differences on the defecation score.

The groups were not significantly different on any of the behavioral measures taken during the minute prior to shock onset in the training session. The predominate activity during this period was generalized activity, each group being rated as active on approximately 80% of the samples. No sample was scored as freezing.

Cat Test

Figure 3B shows the mean percentage of freezing for the three groups in the cat test. Analysis of variance showed that the groups differed significantly in freezing, $F(2,33)=9.58$, $p<0.001$. Post-hoc comparisons showed that the vermal-lesioned group froze significantly less than either of the other two groups, $p<0.05$, and the hemispheric-lesioned and sham-operated groups did not differ significantly. This pattern of differences held for the general activity score, rearing and defecation. The vermal lesioned group was significantly more active, reared significantly more, and defecated significantly less than either of the other two groups, $ps<0.05$. The sham-operated group and the hemispheric-lesioned group did not differ significantly on any measure during the cat test.

The groups were not significantly different on any of the behavioral measures taken during the minute prior to the introduction of the cat. Each group was rated at active on 80–90% of the samples, and no sample was scored as freezing.

DISCUSSION

The results of Experiment 3 replicated very closely our previously reported results [32] on the effects of cerebellar vermal lesions on fear-related behaviors to cats and foot shock. In the presence of a cat, the vermal-lesioned rats gave several indications of being less fearful than controls. They froze less, defecated less, were more active, and reared more. Following foot shock or in the presence of cues associated with foot shock (i.e., the context cues of the test chamber) the vermal lesioned rats did not differ significantly from sham-operated controls on any measure. The present results strengthened our confidence in the cat/shock differences by the basic fact of replication, and they indirectly controlled for possible order effects in the previous report. The cat condition was run after the shock condition in the present experiment, and the reverse order was run previously [32]. As we discussed [32], it is highly unlikely that the shock/cat differences were related to general debilitating effects of the lesions, ceiling effects in the shock condition, or basic changes in the sensitivity to shock. Indeed, the shock/cat differences reduce the possibility that even subtle motor dysfunctions can account for the effects of vermal lesions in this paradigm. In the shock condition, the vermal-lesioned rat produced normally the same response that it was significantly impaired in producing in the cat condition.

The shock test and the cat test differ in too many particulars to allow a complete interpretation of the differential effects of vermal lesions based on present data. It is obvious that the behavioral effects of vermal lesions depend upon the nature of the fear-eliciting stimulus. By comparison, amygdala lesions may produce more general fear effects which are less sensitive to the specific nature of the fear conditions. The results suggest that the cerebellar vermis and the amygdala lie in different positions in a fear circuitry that begins with the eliciting stimulus, proceeds to a central fear state, and continues to a specific kind of response pattern, e.g., freezing.

The effects of the cerebellar hemispheric lesions were not anticipated. We had expected this group to provide a control for any possible general debilitating effects of cerebellar damage, a role the group fulfilled in the cat test. However, the pattern of difference in freezing behavior for the hemispheric-lesioned rats was the reverse of that shown for the vermal-lesioned rats. They did not differ from controls in the cat condition but froze significantly less than controls in the shock condition. It is typically assumed that freezing under the shock-training conditions used here is a Pavlovian conditioned response [16]. Shock is the unconditioned stimulus (UCS), the context of the test chamber is the conditioned stimulus (CS), and freezing is the conditioned response (CR). Viewed in this light the deficit in freezing to foot shock showed by the hemispheric-lesioned rats may reflect a deficit in aversive Pavlovian conditioning. The lateral cerebellum has been shown to be critically involved in Pavlovian conditioning of eyeblink [26,37] and leg-flexion [14] responses in rabbits. There have been no reports of general changes in emotional reactivity or defensive behaviors following lateral cerebellar lesions, the hemispheric lesions did not alter VMH hyperreactivity in Experiment 1, and our subjective impressions of animals with hemispheric lesions suggest none of the changes in emotional responsiveness that are so apparent in the vermal-lesioned rat. Although our data are only preliminary on this point, we suggest that the effects of lesions of the cerebellar hemispheres on freezing behaviors are not related to general effects on agonistic behaviors, as seems to be the case for the medial cerebellum, but rather to specific effects on aversive Pavlovian conditioning. If these effects resulted from impaired conditioning, any aspect of the conditioning process could have been involved, and the present data cannot speak to this issue. However, in the previous reports [14, 26, 37] lateral cerebellar damage did not affect CS or UCS responsiveness, and we found no change in the unconditioned heart rate response to foot shock or tail shock following lateral cerebellar lesions [31].

As discussed above in relation to the vermal lesions, the pattern of results for hemispheric lesions makes explanations in terms of subtle motor dysfunctions very unlikely. In the cat condition the hemispheric-lesioned rat could produce normally the response that it was significantly impaired in producing in the shock condition. If either the vermal or hemispheric lesion effects in this paradigm were related to motor effects of the lesions they would need to be extremely subtle motor dysfunctions which interferred with a particular response only under specific stimulus conditions.

GENERAL DISCUSSION

There can be do doubt that the medial cerebellum is involved in the control of species-specific agonistic behaviors. In the present experiments lesions of the cerebellar vermis attenuated VMH lesion-induced hyperdefensiveness, spontaneous mouse killing, and freezing in the presence of a cat. In previous research medial cerebellar lesions produced taming effects in cats and monkeys [6,29], attenuated septal hyperreactivity in rats [8], altered open field activity and social interactions in ways indicative of reduced defensive behaviors [7,32], and reduced neophobic responses to a novel taste [32]. The developing symptom profile of medial cerebellar damage clearly points to a significant involvement in agonistic behaviors, but the critical dimension of this be-

havioral category is not yet clear. Relating all of the results of medial cerebellar damage to a general reduction in fear motivation fits much of the data but cannot reconcile the absence of a vermal-lesion effect on freezing to foot shock. The cat/foot shock freezing differences may be related to the presence or absence of unlearned, species-specific releasing stimuli, and many of the effects of vermal lesions may be interpreted as related to such stimuli, e.g., the cat, the mouse, dorsal handling contact, or a brightly illuminated arena [32]. However, to the contrary, we have shown that cerebellar vermal lesions block heart-rate conditioning to tail shock or foot shock in rats without affecting unconditioned responses to the shock [31]. At the present time the data only allow us to agree with others (e.g., [5,9]) that the medial cerebellum is involved in the modulation and control of complex, species-specific behaviors. Part of the complexity of the symptom picture may well be related to the size of the lesions which have typically involved a large portion of the vermal cortex or the fastigial nucleus. More discrete lesions of these areas may result in a more limited set of symptoms which could be explained in terms of a single mechanism.

We commented on the similarities between medial cerebellar lesions and amygdala lesions above and previously [32], as have others [9]. The parallels are striking, as are the differences, e.g., cat/shock freezing and learned taste aversions [32]. At this time, we must only insist that the medial cerebellum be included in those brain areas, which include the olfactory bulb, amygdala, septum, hypothalamus, and periaqueductal gray, involved in the control of agonistic behaviors [1–3, 33]. Significant progress in understanding the brain mechanisms of agonistic behaviors will be made as we look more carefully at the interactions among these brain areas and as we more clearly draw distinctions among the various categories of agonistic behaviors.

Throughout these experiments, we have commented on the possibility that some motor impairment, whether a general debilitation or a more subtle dysfunction, might account for the behavioral effects of lesions of the cerebellar vermis. The issue is a critical one given the classical and well established involvement of the cerebellum in the coordination and elaboration of motor activity. We argued above that specific elements of each experiment strained explanations in terms of motor deficits, and the specific outcomes of Experiment 3 were particularly difficult to explain in motor terms. However, it is the overall pattern of results with medial cerebellar damage in these experiments, in our previous work [32], and in the work of others (e.g., [6–8, 29]) that we find most persuasive on this point. The motor and sensory characteristics of these many behaviors vary much too widely to be accounted for in strictly motor or sensory terms, and the data show a consistent, yet complex, pattern specifically related to species-specific agonistic behaviors.

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