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IMPAIRMENTS ON LOCOMOTOR TASK INVOLVING SPATIAL OPPOSITION BETWEEN CUE AND REWARD IN FRONTALLY ABLATED MONKEYS

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In a previous experiment (Stępień et al. 1966) dogs and cats were trained to respond to an auditory cue by walking to a food tray located in the direction opposite to that of the source of the cue or in a neutral place at a distance of 2 m from it. This habit became severely disturbed following bilateral ablation of medial precruciate cortex (which was originally regarded as a part of the premotor area) and the animals exhibited marked "magneto-reactions" during the early post-operative period which only declined gradually during post-operative training. The magneto reaction which was expressed by the subject's approach to the cue, standing in front of it during its activation and often touching it with the nose, could not be elicited by removal of other cortical areas of the frontal lobes, including the proreal areas. Since ablation of these structures have been found to result in severe impairments by dogs on tasks of delayed response (Ławicka et al. 1966) it appears that two distinct patterns of behavioral impairments can be related to these two cortical areas in the dogs frontal lobes. In monkeys impairments on delayed response tasks are clearly elicited by ablation of dorsolateral prefrontal cortex, and especially the segment of sulcus principalis (Mishkin 1957).

The aim of the present investigation is to further explore homologous organization of frontal cortex in dogs and monkeys by training of monkeys on locomotor tasks involving spatial opposition between location of

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cue and reward, and subsequent removal of restricted cortical areas. The specific extent of cortical ablations may then be determined which elicit responses of magneto reactions in monkeys.

METHOD AND PROCEDURE

Subjects. A total of 20 immature rhesus monkeys (*Macaca mulatta*) of 3 to 4 kg body weight were used.

Apparatus. Testing was conducted in an "open field" box, of floor dimensions as indicated by Fig. 1, and inside height of 76 cm. The outside walls are constructed of masonite, painted black, and the three internal vertical partitions dashed lines) are of transparent lucite. At the extreme left and right walls diffuse plastic plaques, 6.3 cm in diameter, are mounted at the monkey's eye level. For presentation of the cues, these are illuminated from the rear by red light of markedly greater brightness than the general diffuse white overhead illumination of the compartment. Loudspeakers are mounted above the plastic plaques for presentation of auditory cues. Food cups are mounted near the left and right ends of the long wall (Fig. 1) above floor level and each cup is covered by a hinged plastic lid, which can be

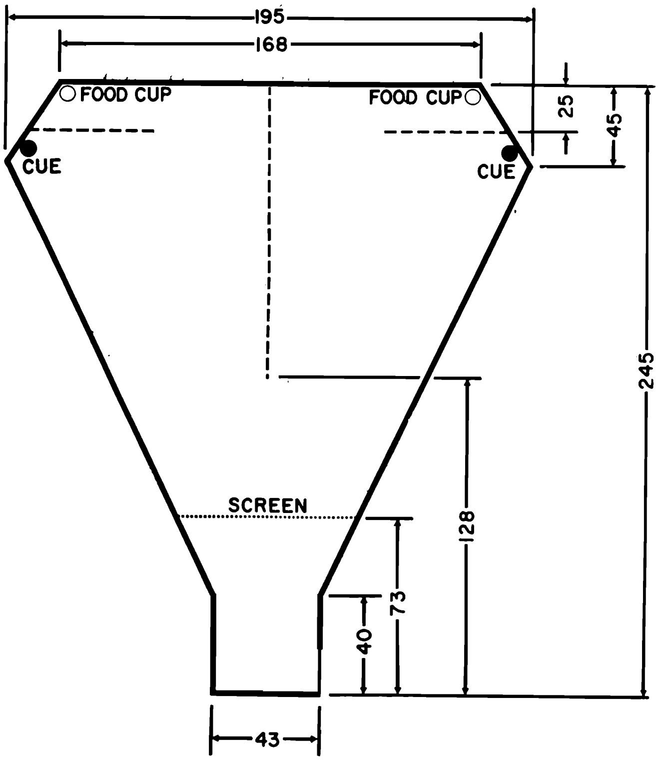


Fig. 1. Open field testing apparatus

raised by the monkey. One-way vision screens are provided, so the experimenter can observe all movements of the monkey.

Surgery. Bilateral cortical ablations were performed during one stage aseptic surgery. The monkey was anesthetized with Nembutal, its head mounted in a holder, and its skin and fascia opened. The appropriate portion of the skull was opened, either with rongeurs or as a bone flap. After opening of the dura, cortex was removed by subpial aspiration with an 18 gauge sucker. Dura was closed with sutures and the skull openings covered with stainless steel screening. Fascia and skin were sutured in layers. The intended limits of cortical resections as indicated by Fig. 2 (sketch of frontal lobe) were.

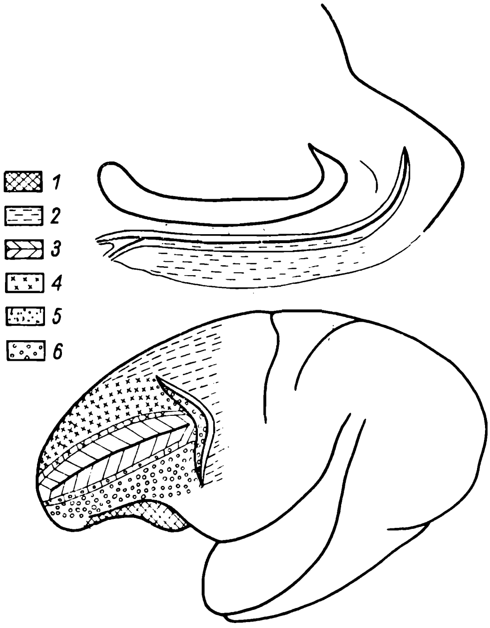


Fig. 2. Mapping of areas within the frontal lobe in monkey. 1, orbitofrontal cortex; 2, premotor cortex; 3, principalis cortex; 4, DAL dorsal cortex; 5, anterior arcuate cortex; 6, DAL lateral cortex

Premotor cortex. The skull was opened by bone flap and after exposure of the frontal lobe it was retracted by placing of small cottonoid patties between the medial aspect of the frontal lobe and the falx cerebri. The medial cortical strip was aspirated between the dorsal surface and depth of cingulate gyrus, and from the beginning of the corpus callosum to central fissure. Dorsolateral cortex was removed between the depth of arcuate sulcus and extensions of its branches to midline and to the orbital edge and a line through precentral dimple and parallel to central fissure. In one monkey (M 127) only the medial portions of this area were ablated.

Orbitofrontal cortex. The frontal lobes were raised with a brain spoon and with patties for visual exposure of orbitofrontal cortex. Cortex was aspirated between midline and the lateral edge, and from frontal pole to the level of junction of frontal and temporal poles.

Dorsolateral cortex. The cortex aspirated was between midline and orbital edge and from frontal pole to depth of arcuate sulcus and extensions of its branches

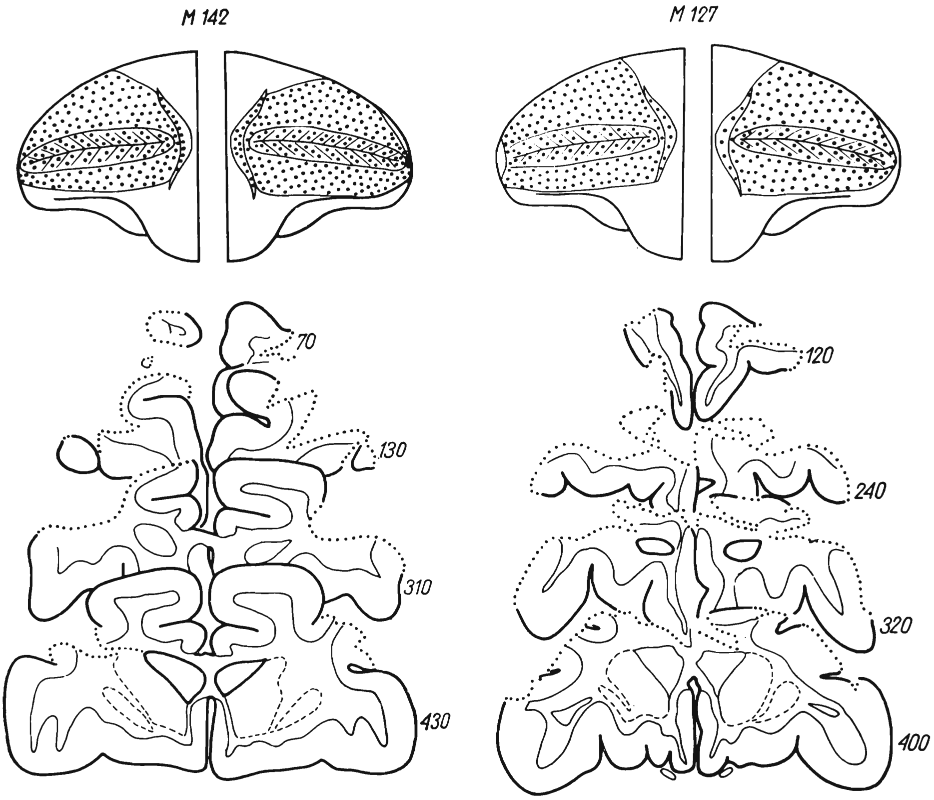


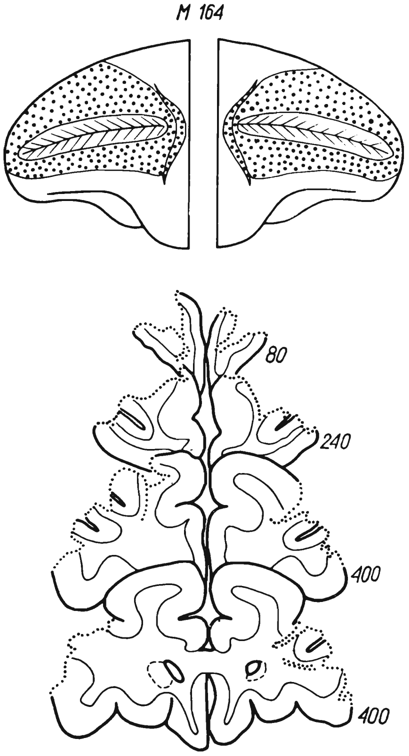
Fig. 3. Extent of cortical removal for four representative monkeys

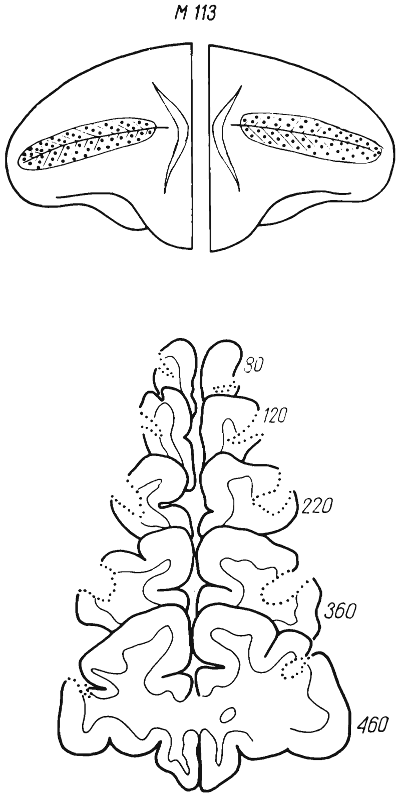
to midline and orbital edge. The principal sulcus was opened, retracted with patties and its banks and depth were aspirated. For M 127 this surgery was performed after the monkey had completed retraining following ablations of supplementary motor cortex.

Principalis cortex. After opening of the principal sulcus, cortical aspiration was limited to its depth and banks, to approximately 2 mm below the dorsal surface.

DAL cortex. Resection spared the area of principal sulcus, but included the dorsal, anterior arcuate, and lateral segments of the dorsolateral surface. Cortical strips, approximately 2 mm wide along the dorsal edges of principal sulcus were spared. Smaller ablations consisted of aspiration of either the dorsal, anterior arcuate, or lateral segments of this area.

Procedure. During preliminary training the monkey was adapted to the apparatus and learned to retrieve peanut kernels from the left and right cups in the testing box. Each subject was then trained, at 30 trials per session, on one of the following tasks, until it met the criterion of 81 correct responses in 90 consecutive trials. For most subjects only visual stimuli were used, while a few monkeys were trained only with auditory stimuli. Table I indicates the surgical group to which each monkey was assigned and the task on which it was trained.





Task I. While the monkey was in the starting compartment one stimulus was activated, generally for 2 sec duration. The monkey was rewarded (with a peanut kernel) for a response to the food cup located on the opposite side of the stimulus, whereas responses to the other food cup or to the cue, or its remaining in the starting compartment were scored as incorrect. On successive trials the stimuli were presented on the left or right side according to a random sequence, with 15 presentations to each side in a session.

Task II. The stimuli were presented according to the same sequence as for Task I, but rewards were only presented to the right food cup, regardless of the source of the cue.

Task III. The same sequence of stimulus presentation was followed as for Task I, but rewards were presented in the food cup located next to the source of the stimulus.

After a monkey had met criterion on a task it was given 10 days of rest and then after retention testing it was subjected to one stage bilateral surgery. Post-operative training was resumed 10 days after surgery and continued until the monkey reattained criterion performance or for 1980 trials. M 127 was the only monkey which received a second cortical ablation, following its reattainment of criterion.

Anatomy. After completion of post-operative testing the monkey was perfused with saline and 10% formaline solution. The brain was processed according to the celloidin technique and sectioned at 30 μ. Every 20th section was stained with buffered thionin. The sections were projected through an enlarger and traced for reconstruction of the lesioned areas.

RESULTS

Fig. 3 shows the extent of cortical removal for four representative monkeys which had received total or partial ablations of dorsolateral prefrontal cortex.

The behavioral results are summarized by Table I and representative rates of error responses are shown by Fig. 4 and 5. The consequences of the cortical ablations were.

Orbitofrontal cortex. Correct performance by the monkeys in this group was little affected by the cortical ablations. Post-operative criterion was attained by M 111 during the second (Fig. 4) and by M 123 (which had previously received bilateral amygdalectomy) during the fourth session with visual cues. With presentation of acoustic stimuli M 129 reattained the criterion somewhat slower, since it responded at approximately 80% correct during sessions 4—7, before reaching criterion level.

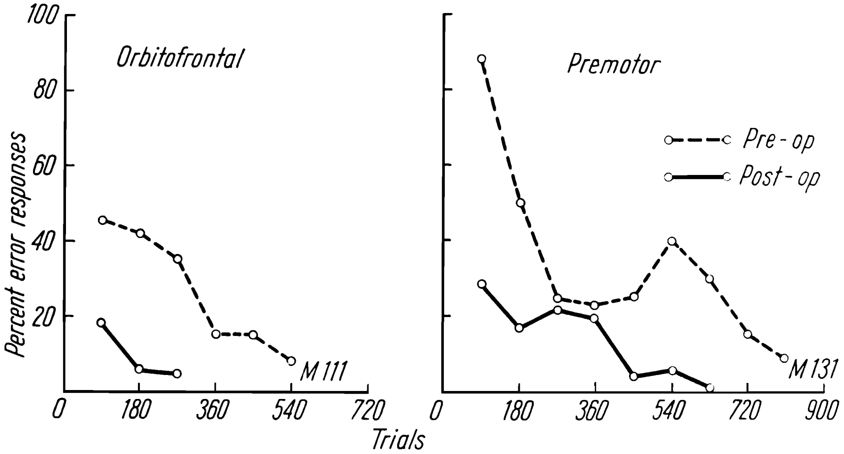


Fig. 4. Error responses for two monkeys during pre- and post-operative training on task of spatial opposition

Premotor cortex. Ablation of premotor cortex had little effect on the monkey's correct performance on the tasks, as indicated by Fig. 4 for

Table I

Summary of results

Cortical Ablation	Monkey	Task[a]	Total errors		Response to cue (% of errors)	
			Pre-op	Post-op	Pre-op	Post-op
Orbitofrontal	111	I—Vis	71	23	23	9
	123[b]	I—Vis	278	92	2	22
	129	I—Ac	226	130	12	8
Premotor	127	I—Vis	202	9	9	0
	131	I—Vis	304	67	11	6
	139	II—Vis	19	13	0	17
Prefrontal (total dorsolateral)	127	I—Vis	202	640	14	36
	128	I—Vis	300	735	9	8
	134	I—Vis	148	456	6	31
	135	I—Ac	439	1455[c]	21	5
	143	II—Vis	37	159	40	88
	142	III—Vis	6	5	0	0
	162	III—Vis	9	14	0	0
Principalis	113	I—Vis	369	21	9	0
	170	I—Vis	305	46	18	0
DAL[d]	161	I—Vis	312	387	12	22
	164	I—Vis	285	421	0	21
Dorsal Anterior arcuate Lateral	168	I—Vis	191	86	7	5
	165	I—Vis	365	67	16	0
	172	I—Vis	261	3	17	0
	174	I—Vis	304	3	5	2

[a] Task I, Spatial opposition between stimulus and reward;
II, Stimulus left or right, reward in same cup;
III, Stimulus and cup on same side;
Vis, Visual stimuli; Ac, acoustic stimuli.

[b] Before the orbital ablation the amygdalectomy was made.

[c] Failure to meet criterion.

[d] Dorsolateral cortex surrounding sulcus principalis.

M 131 which had received extensive resection of both dorsolateral and medial aspects of premotor cortex. The premotor monkeys succeeded in responding correctly, in spite of their severe difficulties of bodily balance and coordinated movements. Their movements were poorly coordinated, slow, and awkward. By contrast, the monkeys in the other surgical groups exhibited well coordinated and smooth movements. M 127 whose lesions were restricted to the medial cortical strips, responded without any errors during the first 90 post-operative trials. On the simpler Task II, M 139 remained unimpaired after the extensive premotor ablations.

Dorsolateral prefrontal cortex. As indicated by Table I, and by Fig. 5 for M 127, resection of dorsolateral prefrontal cortex markedly impaired the monkey's ability to perform correctly on Task I. Although the three subjects which were trained with visual stimuli were eventually able to reattain criterion, their relearning rates were exceedingly slow and the number of post-operative errors were several times greater than preoperative and those for the monkeys with orbitofrontal or premotor lesions. The monkey which had been trained with acoustic stimuli (M 135) was unable to achieve criterion after 1980 post-operative trials and did not perform above 70% correct during any session. Marked impairments were also manifested on the much easier Task II, as illustrated by Fig. 5 for M 143. By contrast, the prefrontal monkeys trained on Task III, when rewards were presented at the same side as location of the stimuli, remained unimpaired after prefrontal ablations. The limits of cortical resection for these monkeys (Fig. 3, M 142) were essentially the same as for the prefrontal monkeys that had been trained on the other tasks (Fig. 3, M 134).

Of further significance is the incidence of different types of post-operative error responses. Whereas during preoperative training most of the errors were to the food cup located at the side of the stimulus or remaining in the starting compartment throughout the period of stimulus presentation, a substantial proportion of post-operative errors were responses directly to the visual stimulus, rather than to the adjacent food cup (Table I). For two of the prefrontal monkeys over 30% of error responses consisted in approaching the stimulus light and often touching it.

The tendency to approach the source of the cue was very evident when the stimulus was occasionally prolonged to 10—30 sec. The prefrontal monkeys could oscillate between the starting cage and the source of the cue 5—10 times until the stimulus had been discontinued.

Principalis cortex. Ablations which were restricted to the banks and depth of sulcus principalis, as shown by Fig. 5 for M 113, did not appreciably affect the monkeys correct performance on Task I. The small number of errors which were only made during the first 90—180 trials correspond to those made by monkeys with prefrontal lesions.

DAL cortex. By contrast, ablations of prefrontal cortex which surrounds sulcus principalis resulted in marked impairments on Task I, as illustrated by Fig. 5 for M 161. The scores of total errors for the two monkeys in this group are appreciably higher than those for the princi-

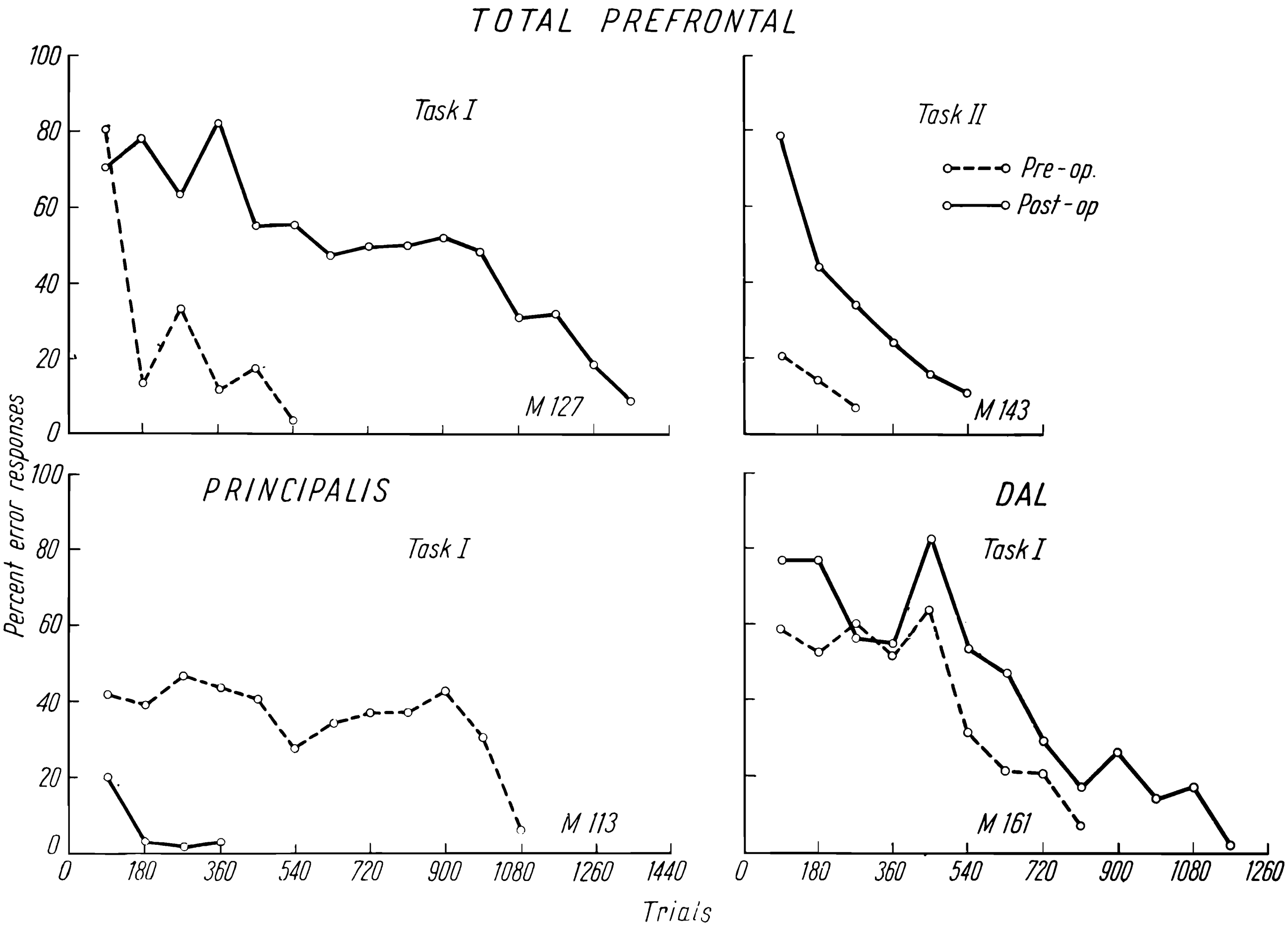


Fig. 5. Error responses for four monkeys during pre- and post-operative training

palis group, but somewhat lower than for the monkeys with total prefrontal ablations. The incidence of error responses directly to the stimulus is also highly elevated (Table I).

Ablations of portions of this cortical area, had only little effect on correct performance. As seen by Table I, monkeys responded essentially at pre-operative levels, regardless of resection of the dorsal, anterior arcuate, of lateral segments of cortex surrounding sulcus principalis.

DISCUSSION

In the present experiment monkeys were trained on a locomotor task of responding to a visual stimulus by approaching a food cup that was located in a place not contiguous to that of the cue. Dogs and cats were found severely impaired on an analogous task after ablations of precruciate cortex (Stępień et al. 1966), an area that is considered as part of premotor cortex. We found that extensive ablations of the monkey's premotor cortex, including the "supplementary motor area" (Woolsey et al. 1950) did not interfere with the animals correct performance, although their postural and motor abilities were severely disturbed. By contrast, removal of dorsolateral prefrontal cortex resulted in severe and long lasting impairments on the task. The well known prefrontal symptom of hyperactivity was manifested by the monkey's running back and forth in the testing compartment, both during the intertrial interval and after activation of the stimulus. In response to the visual stimulus they generally ran to the adjacent food cup and raised its cover. However, three of the five prefrontal monkeys also frequently approached the source of the stimulus once or twice and occasionally briefly touched it. They then returned to the starting compartment. This behavior was rarely observed during pre-operative training when a substantial proportion of error responses consisted in the monkey's remaining in the starting compartment throughout the period of cue presentation. Although the prefrontal monkeys did not remain in front of the stimulus, as had been observed with precruciate dogs, prolongation of stimulus presentation to 30 sec, which was given during several trials, resulted in their repeated returning to the stimulus, as often as ten times. Consequently, the response of the prefrontal monkeys may be considered as a magnetoreaction, analogous to that which had been observed with dogs and cats. This reaction was demonstrated even more clearly on the easier Task II, when rewards were delivered in only one food cup, regardless of the direction of the visual cue. The high rate of error responses exhibited by the prefrontal monkey trained on this task (Fig. 5) is in marked contrast to the correct post-operative performance by two prefrontal monkeys which were trained on Task III, when the reward was delivered to the food cup adjacent to the stimulus.

The findings that precruciate dogs were also severely impaired on the easier task when food was delivered in only one tray, but responded correctly when the reward was delivered adjacent to the stimulus, supports our interpretation of the magneto-reaction being elicited by prefrontal ablations. Consideration should be given, however, to behavioral differences between precruciate dogs and prefrontal monkeys. Post-operatively both species exhibited motor hyperactivity during the intertrial interval, but during the period of stimulus presentation the precruciate dogs were more strongly attracted to the stimulus than were the monkeys and often remained quietly in front of the metronome for as long as one minute. These findings may be the consequence of species differences.

The fact that the number of errors in precruciate dogs' performance could be as high as 100 % while in monkeys it was in the early post-operative period on the level of 70—80 %, may be related to the differing arrangements of the apparatus. The angular separation between the left and right cues was appreciably greater in the experimental situation for the dogs than in that for the monkeys. In the experimental situation for dogs an animal performing a turn toward the source of the cue could see only one foodtray namely that which was located next to the cue. In the situation in which monkeys were tested an animal could see both cups in the same time.

The present results, however, clearly establish that prefrontal ablations result in pronounced magneto-reactions in monkeys, which is indicated by rates of error responses as high as 80 % of the total responses immediately after surgery and only a very gradual decline of error rates during the course of extensive post-operative training. Although the monkeys were able to reattain criterion performance, they required about three times as much training as they had pre-operatively.

Of further significance may be the finding that the magneto-reaction was not elicited after ablation of cortex in sulcus principalis, but was clearly evident after resection of the surrounding dorsolateral cortical areas (DAL cortex). The fact that magneto-reaction in monkeys may be elicited exclusively after ablation of prefrontal area shows that the medial precruciate cortex in dogs belongs to the prefrontal and not to the premotor cortical area as was originally assumed. This supposition is further substantiated by the anatomical findings by Sychowa et al. (1968) indicating that in dogs the medial precruciate lesions are followed by retrograde degeneration in the dorso-medial thalamic nucleus. Accordingly it may be hypothesised that DAL cortex in monkey and the medial precruciate cortex in dog are homologous both functionally and anatomically.

SUMMARY

18 monkeys were trained on locomotor task involving spatial opposition between location of cue and reward. The subjects learned to respond to a cue by walking to a food cup located in the direction opposite to that of the source of the cue.

This habit became severely disturbed following bilateral ablations of the dorsolateral prefrontal area, as well as its part surrounding principal sulcus only (DAL cortex). The lesioned monkeys exhibited marked "magneto-reaction" which was expressed by the subject's approach to the cue and/or the food cup located next to it. The number of such reactions being as high as 70—80% in the early post-operative period diminished gradually in the course of experimentation and dropped to the criterion level at last.

Ablations of other cortical areas within the frontal lobes (depth of principal sulcus; orbitofrontal area; supplementary motor cortex, or premotor area) failed to evoke the magneto-reaction and had only a little effect on correct performance of the task.

Two monkeys being trained on the task when rewards were presented to the food cup next to the cue after dorsolateral prefrontal ablation performed the task on a pre-operative level.

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