Dissociation of Impairment after Lateral and Medial Prefrontal Lesions in Dogs

Abstract. *Dogs were trained before operation on a go, no-go test with symmetrical reinforcement. Lesions situated on the medial surface of the prefrontal cortex caused slight or no impairment in retention, whereas removal of the lateral prefrontal cortex induced severe and long-lasting impairment. The lateral prefrontal cortex is probably related to selection of the proper instrumental responses to corresponding stimuli.*

The so-called go, no-go differentiation test can be applied in two ways. Either the animals are required to react to the positive conditioned stimulus (CS) by performing a trained movement in order to obtain food, whereas the negative CS is never reinforced [go, no-go differentiation with asymmetrical reinforcement (DAR)], or the animal is trained to perform the given movement to the positive CS and not to perform it to the negative CS, both of these stimuli being reinforced [differentiation with symmetrical reinforcement (DSR)].

The effects of prefrontal lesions in dogs trained in the DAR procedure have been extensively studied in our laboratory (*1*). Whereas the go responses to the positive CS are not impaired, the responses to the negative CS are disinhibited. Further studies revealed that lesions limited to the medial aspect of the prefrontal regions (gyrus pregenualis) produce disinhibition of no-go responses, but lesions in the lateral prefrontal areas (gyrus proreus and orbitalis) in general fail to produce this effect (*2, 3*). However, it has been shown that when very short (15-second) intertrial intervals are used, go, no-go differentiation is impaired also after lateral prefrontal lesions (*3*).

We present here studies of the effects of prefrontal lesions with the DSR test in dogs.

Sixteen naive mongrel dogs were trained in the following way. When a tone of 1000 cycle/sec was presented, the animals were required to place the right foreleg on the feeder in order to obtain the food. When a tone of 700 cycle/sec was presented the animals received food only if during 5 seconds of the tone's presentation they refrained from performing the trained movement. Each stimulus was presented ten times in every session in balanced order. Eight animals were trained with 60-second intervals between trials and eight animals were trained with 15-second intervals. When the animals reached criterion (five errors in 100 consecutive trials during five consecutive days) they were divided into two groups and subjected to surgery. In eight dogs the medial aspect of the hemispheres in front of the anterior genual gyrus was removed bilaterally, whereas in the eight others the dorsolateral cortex anterior to the presylvian fissure was removed (Fig. 1). Beginning 8 days after surgery the animals were tested for retention, during which they were required to reach criterion again; if after 800 trials criterion was not attained, retraining was discontinued. After the experiments were completed the animals were killed and the extent of the lesion was examined by routine histological methods.

Lateral lesions produced dramatic impairment of differentiation, affecting equally the animals trained with 15- and 60-second intervals between trials (Table 1). Only one animal (No. 13) reached criterion after 660 trials, whereas the others failed to reach criterion after 800 trials. Although both types of errors were observed in these animals, commission errors were more frequent.

On the other hand, the animals were

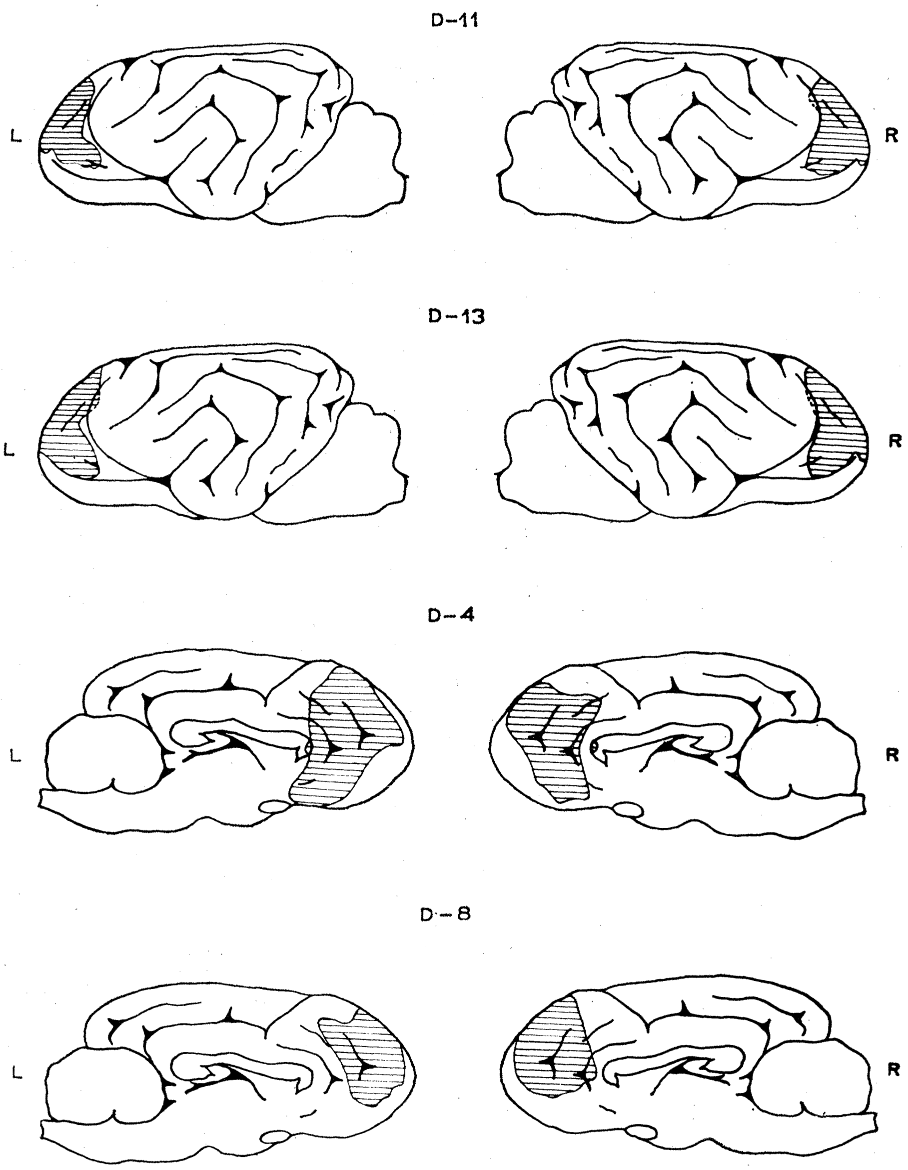

Fig. 1. Representative reconstructions of the prefrontal lesions. (*D-11* and *D-13*) Lateral reconstructions of bilateral ablation of the proreal and anterior orbital gyri in dogs Nos. 11 and 13. (*D-4* and *D-8*) Medial reconstructions of bilateral ablation of the medial prefrontal cortex in dogs Nos. 4 and 8.

Table 1. Number of trials and errors to reach criterion.

Interval (seconds)	Number of dog	Preoperative			Postoperative		
		Trials	Omission errors	Commission errors	Trials	Omission errors	Commission errors
				Lateral lesion			
15	9	820	0	210	800	66	253
15	10	720	0	202	800	6	197
15	11	680	0	217	800	94	232
15	12	500	1	151	800	79	130
60	13	560	0	156	660	84	74
60	14	300	0	72	800	98	185
60	15	440	0	127	800	64	212
60	16	360	0	89	800	105	123
				Medial lesion			
15	1	1280	0	402	100	0	3
15	2	640	0	199	120	0	9
15	3	520	1	149	220	1	28
15	4	740	1	204	280	3	26
60	5	540	0	161	120	0	9
60	6	580	0	236	220	2	26
60	7	600	0	121	160	0	14
60	8	1320	54	225	120	0	7

almost unimpaired by medial lesions. Only three animals (Nos. 3, 4, and 6) did not reach criterion immediately. Histological verification showed that the lesions in these dogs invaded the white matter slightly.

Comparing two analogous series of experiments, one performed with the DAR procedure of the earlier study (*3*) and the other with the DSR procedure in this study, we find that with intertrial intervals lasting 60 seconds, medial and lateral lesions had quite opposite effects. Medial lesions produced impairment on the DAR test, but only very slight or no impairment on the DSR test; on the contrary, lateral lesions produced dramatic impairment on the DSR test, but no impairment on the DAR test. When the intervals between trials were very short (15 seconds), performance in the DAR test was impaired by both medial and lateral lesions, whereas performance on the DSR test was impaired after lateral lesions only.

These results seem to indicate that the DAR and DSR procedures measure two quite different physiological mechanisms. In fact, the DAR test may be regarded as a drive, no-drive differentiation because the no-go response is developed to a stimulus that is never followed by food. Consequently, the disinhibitory effect of the medial lesions in the DAR procedure was attributed to abnormal searching and sniffing activity and excessive conditioned response during intertrial intervals, which suggests that the retention loss of differential inhibition reflects the release of drive functions from cortical inhibitory control (*3*). On the other hand, in the DSR procedure both stimuli are followed by the presentation of food, but the animal must learn that to the positive CS it must perform the trained movement and to the negative CS it must not. Accordingly, the DSR procedure may be regarded as one requiring a differentiation between two movements, flexion of the leg to one CS and extension to the other one. In fact, it could be observed that in response to the negative CS the dogs actively restrained performance of flexion by performing antagonistic movements.

If this interpretation of the DSR test is correct, the lateral surface of the prefrontal cortex may be considered to be concerned with selection of the proper instrumental responses to the corresponding CS's.

In these experiments lateral lesions included both the dorsal aspect of the prefrontal cortex (gyrus proreus) and the lateral aspect (so-called gyrus orbitalis). In more recent experiments, we have found that performance on the DSR test is not impaired after purely proreal lesions, but that it is after orbital lesions. Since proreal lesions produce impairment in the delayed response test (*4*) whereas orbital lesions do not, the conclusion follows that the three tests—DAR, DSR, and delayed response—depend on different prefrontal structures.

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References and Notes

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5. I thank Dr. J. Konorski for helping me in preparing this report and Dr. M. Mishkin for correcting its style. I am also indebted to Mrs. H. Kosmal for the histological analysis of the brains.

14 September 1970; revised 9 November 1970 ■

Development of Polysensory Responses in Association Cortex of Kitten

Abstract. *Sensory responsiveness of single neurons in posterior association cortex of kittens that were 7 to 50 days old was investigated. The percentage of trimodal cells (that is, cells that respond to visual, auditory, and somesthetic stimulation) increased gradually until day 50, when percentages of trimodally responsive cells approached the adult level. In the youngest kittens, cells were predominantly responsive to only visual stimulation. With maturation, responsiveness to auditory and then to somesthetic stimulation was observed in increasing percentages of cells.*

Although the immaturity of kitten cortex has been stressed in anatomical and physiological studies (*1*), several electrophysiological investigations have shown cortical activity in response to specific sensory stimuli. At the single neuron level, Hubel and Wiesel (*2*) have described cells that respond to complex visual stimuli in visual cortex of the 8-day kitten, and Rubel (*3*) reported somatotopic organization of unit cluster activity in sensorimotor cortex of the 1-day kitten. Gross evoked potentials have also been obtained from visual cortex (*4, 5*) and auditory cortex (*4, 6, 7*) in the neonate. Although these responses are characterized by long latencies and long recovery cycles, it appears that primary cortical areas are at least potentially capable of processing