Acta Biologiae Experimentalis, Vol. XIX, 1959

PHYSIOLOGICAL MECHANISM OF DELAYED REACTIONS III. THE EFFECTS OF PREFRONTAL ABLATIONS ON DELAYED REACTIONS IN DOGS

W. ŁAWICKA and **J. KONORSKI**

Department of Neurophysiology, Nencki Institute of Experimental Biology, Warsaw

(Received 3 October 1958)

It has been firmly established that one of the most striking symptoms of prefrontal ablations in monkeys and apes is the disturbance of the delayed responses (Jacobsen 1936, Finan 1940, 1942, Malmo 1942, Wade 1947, Harlow et al. 1952, Pribram et al. 1952, Mishkin and Pribram 1956). Although the fact itself has never been put in doubt, its interpretation has evoked considerable controversy. While the first discoverer of this symptom, Jacobsen, attributed it to the impairment of recent memory (as contrasted with the preservation of permanent memory), other authors connected it with increased distractability of the animals following prefrontal ablation (Malmo 1942, Wade 1947, Harlow et al 1952), to hypermotility (Wade 1947), or to the impairment of associative functions (Nissen et al. 1938, Finan 1942).

In previous papers from this laboratory (Brutkowski et al. 1956, Brutkowski 1957, Ławicka 1957), it has been established that after limited lesions of the prefrontal areas in dogs (involving g. proreus and g. orbitalis), positive alimentary conditioned reflexes are fully preserved while inhibitory reflexes (both classical and instrumental) are greatly disturbed. This disturbance is not permanent, and after some postoperational training the inhibitory ability of the animals is partially, or even completely, restored. It has also been shown that some well known symptoms of prefrontal ablations found by other authors, e.g. the impairment of difficult discriminations (Harlow and Speat 1943, Settlage, Zable and Harlow 1948) etc. can be easily explained by the lack of inhibition (cf. also the article of Stanley and Jaynes 1949).

The problem arose whether the impairment of delayed responses is also connected with the disturbance of inhibitory processes, or whether it constitutes a quite independent symptom. The aim of this paper is, first, to ascertain whether or not the small lesions of prefrontal areas in dogs will also produce the disturbances of delayed reactions, and, if so, what is the character of these disturbances and what may be their physiological mechanism.

MATERIAL AND METHOD

The experiments were performed on 4 dogs which have earlier (1—2 years ago) been subjected to prefrontal ablations. All these dogs had been used previously in experiments with conditioned reflexes and the symptom of disinhibition after prefrontal ablation was clearly seen in them. The behaviour of these dogs in the delayed response situation was carefully studied and compared with the behaviour of normal dogs described in part II of this series of papers (Ławicka 1959). In two other dogs, the experiments with delayed responses began before the prefrontal ablation, so that their behaviour before and after operation could be compared.

The experimental setting in the present study was exactly the same as that used in the study with normal dogs (Ławicka 1959). Buzzers and lamps fixed on the three foodtrays were used as preparatory stimuli, and unleashing served as the natural releasing stimulus. The length of the delay periods together with the effects of various disturbing factors were studied. After a careful investigation for over 1 year, the dogs were sacrificed. Histological examination of the brains is in progress.

RESULTS

The preliminary training of the prefrontal dogs did not differ from that of normal dogs. They very easily became accustomed to the experimental situation and learned to run to the appropriate foodtrays, first at the click of the moving bowl and then at the preparatory signal. As was observed in part II of this series, the normal animals experienced at the beginning of training some difficulties in locating the source of visual preparatory stimulus (lamp), and gradually learned to scan the foodtrays and see where the visual stimulus came from. The same phenomena were observed in our prefrontal dogs. They also learned to scan the foodtrays and

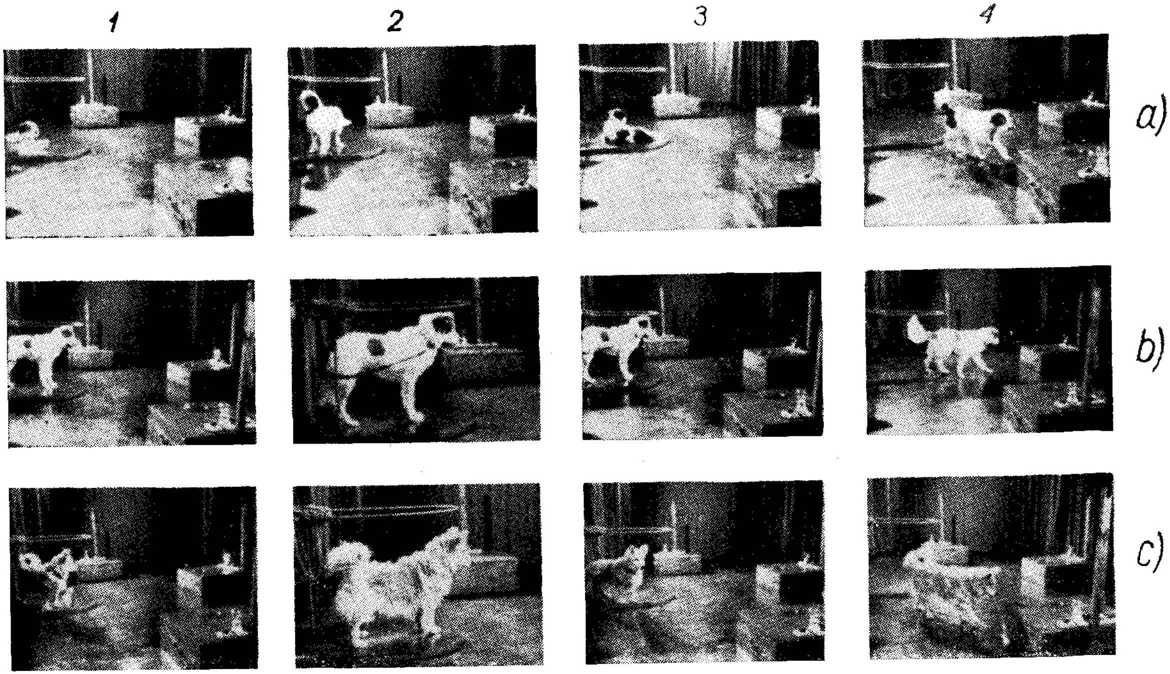

Fig. 1. The behaviour of dogs during the delay period, delay 3 minutes; a — the typical behaviour of normal dog; b and c — the typical behaviour of two prefrontal dogs

1 — the moment of the action of the preparatory stimulus — buzzer; the place of the buzzer is indicated by the lighting bulb: in a the right foodtray is signalled, in b and c, the middle one; 2 and 3 — various moments of the delay periods; in a normal dog behaves quite freely being turned in various directions; in b the dog is turned towards the signalled foodtray throughout the delay period; in c he is first turned to the proper foodtray (2) but then changes his bodily orientation (3); 4 — post-delay reaction: in a and b the dog goes to the proper foodtray, in c he goes to that to which he has been lastly turned

were in this respect not worse than the normal animals. The only difference between the operated and the normal dogs in the preliminary training was that some of the prefrontal dogs manifested an increased tendency to look into other foodtrays in search of food at the end of each trial.

The orienting reaction to the preparatory stimuli was in these dogs also quite normal, and if the delay was short they easily found their way to the proper foodtray. But when the delay periods were prolonged to a minute or more the striking defect characteristic of those animals was manifested. As shown in part II of this series, the normal dog behaves during the delay period quite freely, and finds his way to the proper foodtray independently of his bodily orientation. By contrast with the normal animals, the prefrontal dogs were able to go to the proper foodtray only if at the moment of release they were turned towards it. When during the delay period they had changed their bodily orientation, they went to that foodtray to which they were directed at that moment. In consequence, their performance was much worse than that of the normal dogs, and this was particularly clearly seen under conditions which caused a change in their bodily orientation (Fig. 1).

Length of delay

At the beginning of the experiments with delayed reactions, the prefrontal animals were very poor in their performance. When

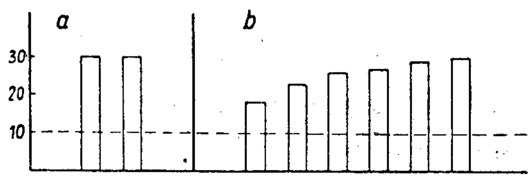

Fig. 2. Gradual improvement of delayed reaction in a prefrontal dog due to learning to keep the bodily orientation during the delay period unchanged. Delay 1 minute; the columns denote the numbers of correct responses in blocs of thirty trials a) before operation, b) after operation. Note the increasing numbers of correct responses in succesive blocks after operation

the animal was released immediately after the application of the preparatory stimulus, or after several seconds, his reactions was correct, but if the delay period was longer, the chance of changing his posture increased and, therefore, he was more and more prone to make mistakes. It was observed, however, that in the course of experiments the animals gradually learned to keep their bodily orientation unchanged during the delay period and, therefore, they were able to react correctly even after longer delays (Fig. 2).

As has been stated elsewhere (Brutkowski et al. 1956), the dogs with limited prefrontal lesions (not extending beyond the presylvian gyrus) are never hyperactive. They are able, therefore, quite easily to preserve their bodily orientation even for a number of minutes. And so, those dogs who were generally more quiet, were able to react properly even if the delay period amounted to 6 minutes. On the other hand, those dogs who were generally more excited were less able to maintain their posture unchanged for

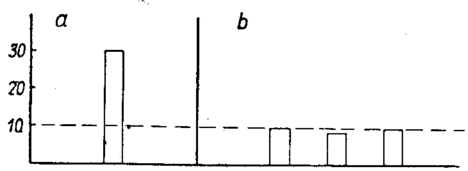

Fig. 3. The effects of disturbances (presentation of food during the delay period) before (a) and after (b) prefrontal ablation. Each column denotes the number of correct responses in blocs of thirty trials with 1 minute delay. Note the lack of any disturbance of the delayed response before operation and the chance level of the response after operation

several minutes and, therefore, they made more mistakes.

In those dogs trained to both visual and acoustic preparatory stimuli the difference between the reactions to these two sorts of stimuli was observed. Since the visual preparatory stimuli elicited in general a weaker orienting reaction than did the acoustic stimuli, the bodily orientation in the correct direction lasted for a shorter time, and in consequence the post-delay reactions to buzzers were better than those to lamps.

Disturbing factors

As indicated in part II of this series, all our normal dogs were exceedingly resistant to various sorts of distracting stimuli applied during the delay — screening, offering food on the starting platform, taking the dog out of the room, etc. The prefrontal dogs were in most cases unable to react properly after these distractions: they went to that foodtray to which they happened to be turned

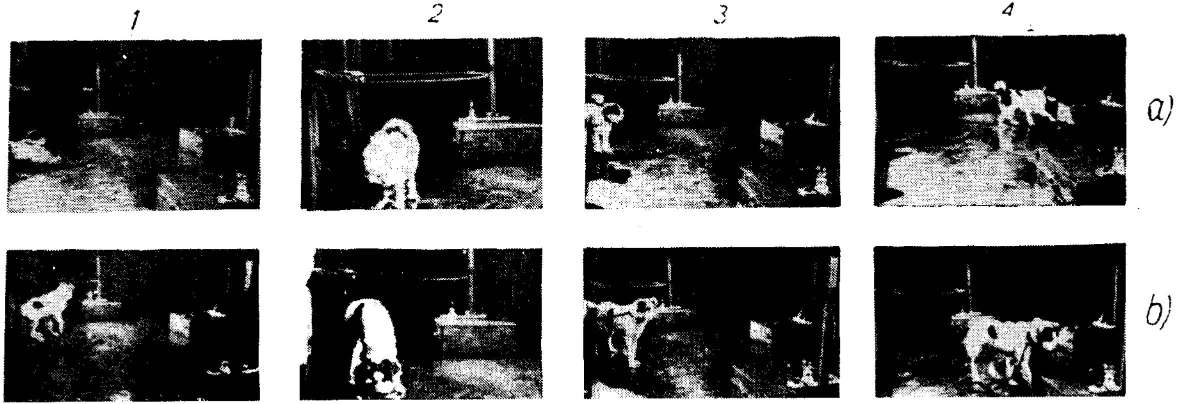

Fig. 4. The disturbance during the delay period: a, normal dog, by prefrontal dog

1 — the moment of the action of the preparatory stimulus; in a the middle foodtray is signalled, in b the left one; 2 — the dog receives food on the starting platform; 3 — the moment after food has been eaten; note that the prefrontal dog changes his position; 4 — the post-delay reaction: the normal dog goes to the proper foodtray, the prefrontal dog goes to the wrong one

at the moment of unleashing, or, sometimes, they remained on the starting platform and went nowhere. Only in those cases in which the distracting stimulus was weak and evoked no more than a turn of the animal's head without change of posture, was the attitude of the dog towards the given foodtray not disturbed, and his post--delay reaction correct (Fig. 3 and 4).

DISCUSSION

Our findings make it quite clear that in the delayed-response test there is a striking difference in the behaviour of normal and prefrontal dogs. This difference is not quantitative, i.e. it does not consist simply in the worse performance of animals after operations, but it is qualitative, since the prefrontal animals behave in a different way from the normal ones. As was seen in part II of this series, normal dogs (as well as cats) do not preserve the bodily orientation to the source of the preparatory stimulus during the delay period. It can be positively stated that the choice of the direction of their run does not, whether correct or incorrect, depend at all on the position held at the moment of release. On the other hand, it seems that in prefrontal dogs the only cue which determines the direction of the run is the bodily orientation, and that the correctness of the run depends on whether this orientation was preserved throughout the delay period. In consequence, all those distracting factors which cause a change in this orientation make the correct run of the prefrontal animal impossible. But if the animals are undistracted, they can preserve their bodily orientation unchanged even for many minutes, and hence they can quantitatively approximate the performance of normal animals.

Thus we conclude that prefrontal animals are guided in the delayed-response situation not by the trace of the preparatory stimulus but by the actual orientation of the body. Accordingly, we call the way in which they solve this task a pseudo-delayed reaction, as contrasted with the true delayed reaction shown by normal dogs. As already observed, the difference between the two modes of behaviour is so clear that there is no difficulty at all in distinguishing them.

It was explained in part I of this series that the true delayed response is based on the ability of the animal to preserve the traces of the preparatory stimulus, or rather of some aspect of it.

The physiological mechanism of these traces was thought to be the activity of reverberating chains of neurons, which continues after the cessation of the actual stimulus. The fact that in prefrontal dogs the ability to keep these traces is obliterated suggests that these reverberating chains of neurons are situated in the prefrontal area. Thus, after removal of this area the animal is able to react properly to the stimulus (either external or postural) during its action, but is lost when this stimulus is discontinued.

We think, therefore, that the original Jacobsen's view that prefrontal ablation destroys the recent memory of the animal is, in fact, correct — but subject to one essential reservation. In the delayed-response tests, we have to do only with recent memory traces of the direction determining „where to go" after the release. It does not follow from this that any other sorts of recent memory are also destroyed by prefrontal ablation.

The prefrontal area represents one of the so-called associative areas which is, topographically, situated just in front of the so-called premotor area. According to the data collected in this laboratory (Stępień et al. 1959) the premotor area (probably in connection with caudate nucleus) controls the gross bodily orientation in space, whereas the sensorimotor cortex is concerned with discrete motor reactions of limbs. It may, therefore, be supposed that the prefrontal association area represents an adjunct to the premotor cortex, and that its role is precisely to maintain the traces of its activity by means of reverberating circuits attached to it.

As observed at the beginning of this paper, the impairment of the delayed responses after prefrontal lobectomies has been explained by various authors by reference to certain other mechanisms — increased susceptibility to retroactive inhibition, hyperactivity, or a defect of associative function. It is clear that the defects in delayed responses found in our experiments cannot be attributed to any of these factors. Our dogs did not exhibit any tendency to an increased activity: they were able to stay motionless throughout the period of delay, which lasted several minutes. Neither did they display a very high distractibility: it was often observed that not too strong extra-stimuli failed to divert an animal's orienting reaction. Moreover, we observed no impairment of associative function in our dogs — they were as capable of learning new motor tricks as were normal dogs.

It is obvious that our prefrontal dogs seemed to perform the delay task much better than did the prefrontal monkeys used in experiments by other authors. This difference may be due to the following factors: First, in our method the foodtrays were situated at considerable distances from one another, while in the generally used Wisconsin Test Apparatus the sources of food are situated in close proximity. Secondly, as shown by Jacobsen, screening ordinarily used in such experiments represents an important distracting factor. Thirdly, the prefrontal ablations performed in monkeys and dogs are not quite homologous. In a subsequent paper we shall show that the more extensive prefrontal lesions in dogs, encroaching on the anterior sigmoid gyrus, still further deteriorate the performance of the delayed responses.

The problem arises why the prefrontal dogs stay motionless fixing the signalled foodtray even for several minutes while the normal animals behave quite freely during the delay period without any stable postural attitude. The fact that usually, in the early experiments, the animals make more errors with long delays than in later experiments suggests that they gradually *learn* to preserve the bodily orientation for progressively longer periods. This learning is closely connected with their essential defect, because every changing of posture leads to a wrong run which is not reinforced by food.

In previous papers from this laboratory concerning the effects of prefrontal ablation it was shown that one of the most striking symptoms of this operation is the disinhibition of the inhibitory alimentary conditioned reflexes. This symptom is usually transient, and with lapse of time the inhibitory ability of the animals is gradually restored. The symptom described in this paper is, on the contrary, permanent: Even after a long period of experimentation, the animals were not able to perform the true delayed reaction. Whether or not these two symptoms — impairment of inhibitory processes and loss of the ability to perform true delayed responses — are functionally or topographically interconnected is a matter for further research.

SUMMARY

1. An investigation of the performance of dogs with limited prefrontal lesions (involving g. proreus and orbitalis) in the triple delayed-response test is presented.

2. It is shown that the prefrontal animals are able to go to the correct foodtray in the post-delay run only if they have, throughout the delay period, preserved their bodily orientation towards that foodtray. If during this period the bodily orientation has been changed, they go, on release, to that foodtray to which they are immediately turned.

3. The animals are able to learn to keep their bodily orientation unchanged during the delay periods, and thus their performance in the course of experimentation gradually improves.

4. All those distracting stimuli which provoke a sufficiently strong orientation reaction to change the animal's posture inevitably disturb the post-delay reaction: after release, the animal runs in the direction which was imposed on him by the distracting stimulus.

5. The mechanism of the impairment of the delayed-response performance in prefrontal dogs is discussed.

We should like to thank Prof. L. Stępień very much for performing operations in dogs used in this study.

REFERENCES

BRUTKOWSKI S., KONORSKI J., ŁAWICKA W., STĘPIEŃ I. a. STĘPIEŃ L. 1956 — The effect of the removal of frontal poles of the cerebral cortex on motor conditioned reflexes. Acta Biol. Exp. *17*, 167.

BRUTKOWSKI S. 1957 — The effect of the prefrontal lobectomies on salivary conditioned reflexes in dogs. Acta Biol. Exp. *17*, 327.

FINAN J. L. 1940 — An analysis of frontal lobe function in monkeys by means of two „delayed response" methods. Psychol. Bull. *37*, 96.

FINAN J. L. 1942 — Delayed response with pre-delay reinforcement in monkeys after the frontal lobes. Amer. J. Psychol. *45*, 202.

HARLOW H. F., DAGNON J. 1943 — Problem solution by monkeys following bilateral removal of the prefrontal areas. I. The discrimination and discrimination reversal problems. J. Exp. Psychol. *32*, 351.

HARLOW H. F., SPEAT T. 1943 — Problem solution by monkeys following bilateral removal of the prefrontal areas. IV. Responses to stimuli having multiply sign values. J. Exp. Psych. *33*, 500.

HARLOW H. F., SETTLAGE P. H. 1948 — Effect of extirpation of frontal areas upon learning performance of monkeys. The Frontal Lobes. Baltimore, Chapter XIX.

HARLOW H. F., DAVIS R. T., SETTLAGE P. H., a MEYER D. R. 1952 — Analysis of frontal a. posterior association syndromes in brain-damaged monkeys. J. Comp. Physiol. Psychol. *45*, 5.

JACOBSEN C. F. 1936 — Studies of cerebral functions in primates: I. The functions of the frontal association areas in monkeys. Comp. Psychol. Monographs. *13,* No 3.

KONORSKI J. and ŁAWICKĂ W. 1959 — The physiological mechanism of delayed reactions. I. The analysis and classification of the delayed reactions. Acta Biol. Exp. *19,* 173.

ŁAWICKA W. 1959 — The physiological mechanism of delayed reactions. II. Delayed reactions in dogs and cats to directional stimuli. Acta Biol. Exp. *19,* 197.

ŁAWICKA W. 1957 — The effect of the prefrontal lobectomy on the vocal conditioned reflexes in dogs. Acta Biol. Exp. *17,* 317.

MALMO R. B. 1942 — Interference factors in delayed response in monkeys after removal of frontal lobes. J. Neurophysiol. *5,* 295.

MISHKIN M. and PRIBRAM K. H. 1956 — Analysis of the effects of frontal lesions in monkeys: II. Variations of delayed response. J. Comp. Psychol. Physiol. *49,* 36.

NISSEN H. W., RIESEN A. H., NOWLIS V. 1938 — Delayed response and discrimination learning by chimpanzees. J. Comp. Psychol. *26,* 361.

PRIBRAM K. P., MISHKIN M., ROSVOLD H. E. a. KAPLAN S. J. 1952 — Effects on delayed-response performance of lesions of dorsolateral and ventromedial cortex of baboons. J. Comp. Psychol. *45,* 565.

SETTLAGE P. H., ZABLE M., HARLOW H. F. 1948 — Problem solution by monkeys following bilateral removal of the prefrontal areas. VI. Performance on tests requiring contradictory reaction to similar and identical stimuli. J. Exp. Psych. *38,* 50.

STANLEY W. C., JAYNES J., 1949 — The function of the frontal cortex. Psychol. Rev. *56,* 18.

STĘPIEŃ I. 1956 — Wpływ usuwania okolic czołowych mózgu na zachowanie się kotów w labiryncie. Łódzkie Towarzystwo Naukowe. Wydz. III, 45.

STĘPIEŃ I., STĘPIEŃ L. and KONORSKI J. 1959 — The effect of ablations of sensor and motor cortex on the instrumental conditioned reflexes. II. Ablations of motor and premotor cortex. In preparation.

WADE M. 1947 — The effect of sedatives upon delayed response in monkeys following removal of the prefrontal lobes. J. Neurophysiol. *10,* 57.