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Chapter 13

ANALYSIS OF ERRORS BY PREFRONTAL ANIMALS ON THE DELAYED-RESPONSE TEST

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Introduction

THE DISCOVERY MADE BY JACOBSEN (1936) ESTABLISHING THAT DELAYED responses (DRs) are severely impaired after prefrontal lobectomies in monkeys may be considered as a milestone in research concerning the functions of prefrontal areas. It is true that much discussion has developed around the question of how Jacobsen's findings should be explained; however, the fact itself has been confirmed by all the investigators studying the problem. As is well known, discussion originally turned around the question of whether impairment of the DRs was caused by a deficit of recent memory, as Jacobsen claimed, or by some other mechanisms. The explanations proposed by other authors referred to animals' hyperactivity (Wade, 1947) or increased distractability (Malmo, 1942; Wade, 1947; Harlow et al., 1952), or else to the impairment of associative function (Nissen et al. 1938; Finan, 1942), to quote only the most widespread concepts.

Several years ago we undertook the study of the effects of prefrontal ablations on DRs in dogs and cats. This was done in the period after we had already established the disinhibitory syndrome following prefrontal ablations in dogs (dealt with *in extenso* in Chapter 12, by Brutkowski), and the question arose whether the impairment of DRs could be also explained by disinhibition. This required the reproduction of the DR test in the same animals in which the first symptom was found, and if the impairment of this test should be observed also in these animals, then it was hoped that an analysis of it would be easier.

In designing our experiments with DRs we applied a method similar to that originally introduced by Hunter (1913), namely, (1) we used the triple-choice method instead of the double-choice method applied in the studies of the DR deficit after prefrontal lesions; (2) the food trays were placed far from each other, separated by an angle of 60° as viewed from the starting platform; and (3) as preparatory signals, buzzers operating from the respective food trays were used (Figure 13.1). The triple choice permitted an analysis of the character of the erroneous responses to be made, since it allowed the animal a double choice between two food trays not signaled by

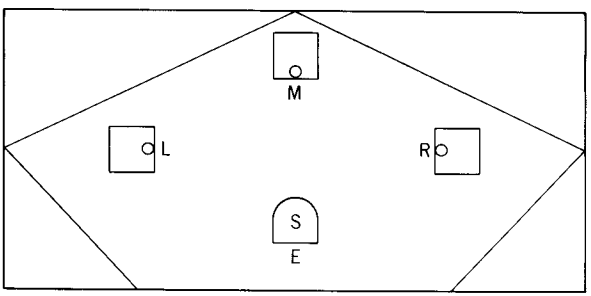

Figure 13.1. Experimental situation for experiments with delayed response. *L, M, R,* left, middle, right food tray. *S,* starting platform. *E,* place of experimenter.

the preparatory stimulus. The large angles between the food trays permitted us to observe the postural reactions of the animal during the delay period. The introduction of buzzers as preparatory signals made the whole experimental procedure in many respects analogous to that used in conditioning experiments.

To give some more details concerning the experimental technique, it should be mentioned that during the delay period the dog was on a leash and the cat in a small cage on the starting platform, while during the intertrial intervals the animal moved freely around the room; in each session the same number of reinforced trials (usually four or five) were given with respect to each food tray; when the animal made an error, it did not receive food in that trial even if it made a "correction" by running immediately to the proper food tray; however, on the next trial the same food tray was signaled, and the animal was released immediately after its presentation, so as to secure a correct response.

Both dogs and cats mastered the rules of the "game" very quickly, and usually after a few preliminary experimental sessions they were fit for regular experimentation.

Our first results obtained on dogs with prefrontal lesions by this method can be briefly summarized as follows (Lawicka & Konorski, 1959):

While normal dogs are amazingly skillful in the performance of the DR test, being able to withstand successfully delays of many minutes and various distractions interposed during the delay period, after the ablation of the prefrontal poles rostrally to the presylvian sulcus, the animals become severely incapacitated in this respect. Their correct response becomes largely dependent on the preservation of their bodily orientation assumed in the moment of the action of the preparatory signal. This orientation being changed, the animal is in most cases not able any more to find his way to the proper food tray. In consequence, all distractions producing a change of the bodily orientation cause, as a rule, erroneous responses. Since the deficit of the animals is not due to increased hyperactivity, our prefrontal animals not being hyperactive, nor to an impairment of associative function, which proved to be quite normal, our first assumption was that the original idea put forward by Jacobsen was right, i.e., the deficit in recent memory in prefrontal animals was responsible for the impairment of their performance in the DR test. The only reservation we made was that not recent memory in general was impaired after the prefrontal lesions, but only the recent memory of *directional cues* (Lawicka & Konorski, 1959; Konorski, 1961a).

However, our further experiments performed on cats with similar technique cast some doubt on this latter interpretation (Lawicka & Konorski, 1961). It had been thought that after prefrontal ablations cats should be rather worse in their DR performance than dogs were, since they were not in the habit of pointing motionless in one direction for long periods of time. What appeared was in fact quite the reverse. First, it was found that cats were able to find their way to the proper food tray after the delay period in spite of the fact that they did not keep their bodily orientation in its direction. Nevertheless, their performance was much worse than that before operation because they made many *perseverative errors*. The following types of these errors could be distinguished: (1) "last response errors" consisting in repeating the last successful response, and (2) "preference errors" consisting in the increased tendency to run to one or two particular food trays. Secondly, after committing an error, the cats very often attempted to correct themselves and ran to the proper food tray, where they remained for a considerable time waiting for the presentation of food (which, of course, was not offered to them). Thirdly, in the course of experiments the cats gradually improved their performance by being more and more able to inhibit their perseverative tendency.

These findings have clearly invalidated the Jacobsenian interpretation of

the DR deficit after prefrontal lesions, at least as far as cats are concerned. However, it was hardly acceptable that a deficit of the same function would have a quite different mechanism in cats and dogs. Therefore, it was necessary to reexamine the DR impairment in dogs in order to see whether the same mechanism of this impairment is here in operation as that discovered in experiments with cats.

The clearest finding obtained in the DR performance in our prefrontal dogs was the deleterious effect of distractions applied during the delay period. It had been found that while without distractions the animals could solve this test even after delay periods of several minutes, owing to their ability to preserve bodily orientation toward the proper food tray, any distraction producing a change of this orientation momentarily reduced their performance to the chance level. It was further proved that this impairment was permanent, at least in our experimental condition. Therefore, it was thought that this type of experiment was suitable for our analysis.

Experimental Evidence

We present here a detailed analysis of a long series of experiments with distractions performed on one of our dogs. Before operation this dog was carefully studied in many DR tests and his performance, even in the most difficult tasks, was excellent. After operation he gradually learned to react properly after a 1-min delay, but this was because he had acquired a habit of facing motionless toward the proper food tray throughout the delay.

In the present series we applied a distraction which had been frequently used before since it appeared to be most convenient for several reasons. The distraction procedure was as follows: 15 sec after the operation of the preparatory signal (the buzzer on the given food tray sounding for 3 sec) a bowl with food was placed on the platform, and small pieces of food were dropped into it by the experimenter for the next 15 sec. The animal had to turn his back to the food tray while eating food, losing any previously assumed bodily orientation. After a further 30 sec the animal was released. If he went to the proper food tray, the trial was completed and a new distraction trial started after 2 min. If his run was wrong, then after 2 min a correction trial was given in which the dog was released immediately after the sounding of the same buzzer. Of course in such a case the animal always reacted correctly. Only then after a 2-min interval was another trial with distraction given.

It is clear that such a distraction could be applied indefinitely since the animal did not become habituated to it and had to change his bodily orientation for the period of eating.

In Figure 13.2 the whole period of experimentation in which distractions were applied is represented. Each block of four sessions with distractions (each session consisting of 15 reinforced trials) was alternated with a similar block without distractions. We can see that while performance on the blocks without distractions in this period of experiments approached almost 100 per cent correct responses, in the blocks with distractions the performance is on the chance level, and does not improve in the course of experiments.

If we analyse, however, the errors the animal committed in more detail, we may see that his responses were far from being random. As seen in Figure

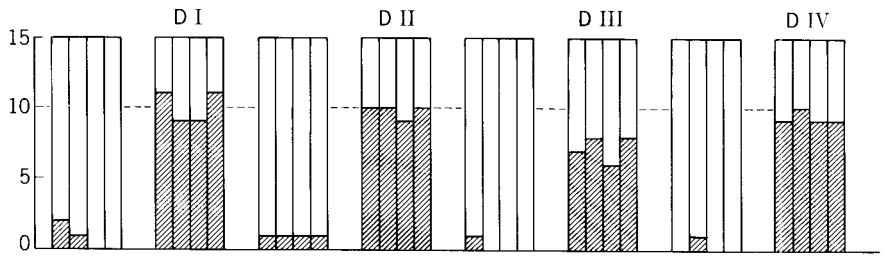

Figure 13.2 The whole course of experiments in a dog described in text. Each bar denotes one experimental session (15 trials). Hatched parts of bars denote the number of trials with incorrect responses. The correction trials with zero delay period are not included. The blocks consisting of four experimental sessions (60 trials) with, and without, distractions were given in alternating sequence. Altogether four blocks with distractions were given denoted as D I, D II, D III, D IV.

Note that in this period of training the responses in sessions without distractions are almost 100 per cent correct, while those in sessions with distractions are on the chance level (interrupted line).

13.3, in which the erroneous responses to various food trays in each block are represented, the animal very quickly developed severe perseveration consisting mainly in approaching the left food tray. Thus, whenever this food tray had been signaled by the preparatory stimulus, the animal's response was correct, but when other food trays were signaled, the response was wrong. This was the cause of two-thirds erroneous responses and the apparent chance level of the animal's performance. It is further seen that at the beginning and at the end of the series, the animal sometimes, instead of going to the wrong food tray, simply went nowhere.

It should be noted that with two other dogs on which a series of experiments with distractions was performed the results were quite the same, except that these dogs preferred the right food tray.

Such behavior shows that the animals found a kind of pseudosolution of the task they were confronted with: the fact that five times in each session

runs to the left food tray were reinforced equalized the whole experimental setup to that of irregular reinforcement, that is, a situation in which, as is well known, the response becomes very resistant to extinction.

In view of the results obtained in our experiments with cats it was assumed that the task presented to the dog was not unsolvable for him, but rather made more difficult, and therefore the animal reverted to the simpler, although less effective, solution of always running to the left food tray. In

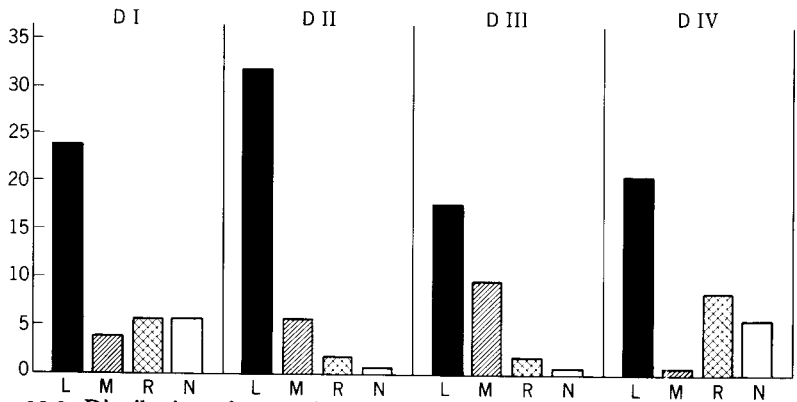

Figure 13.3. Distribution of errors in experiments with distractions. Each group of bars corresponds to four successive sessions with distractions (60 trials) as indicated in Figure 13.2. Each bar denotes the total number of erroneous runs to a particular food tray: *L* (black), *M* (hatched), *R* (cross-hatched) bars denote runs to the left, middle, and right food tray; *N*, no response. Note that the overwhelming majority of erroneous runs are to the left food tray.

consequence, if we could find a way to inhibit this habit, then perhaps the proper solution of the problem could be achieved.

One of the ways of inhibiting the habit of going to the left food tray in trials with distractions would be simply to stop applying the left preparatory signal. In this way runs to the left food tray would never be reinforced and so would be subjected to regular extinction. This method was indeed used with success in one of the series of experiments performed on a prefrontal cat, as may be seen in Figure 13.4. However, it was thought that it would be more profitable to preserve the triple-choice method, and assure a more comprehensive analysis of errors committed by the animal. Taking this into account another procedure was adopted which ran as follows:

After each successful response in trials with distraction, a number

of "sham trials" were given: the animal being attached on the platform received food in the bowl, exactly as in the trials with distractions, and then, after 30 sec, he was released. In other words the sham trials differed from the true ones in that no preparatory signal was given.

Here at once a clear difference between the prefrontal dog and a normal one became manifest. While a normal dog in the absence of a

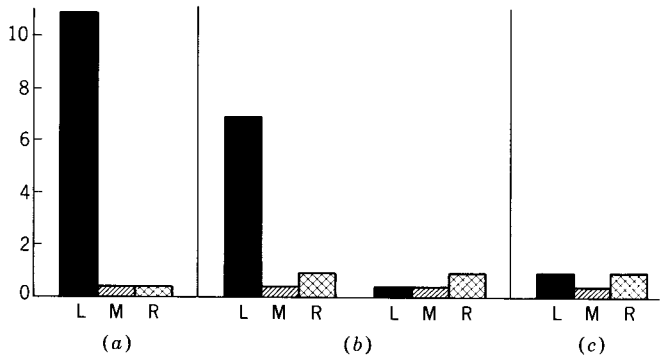

Figure 13.4. A series of experiments with a prefrontal cat, where preferential responses to one food tray were extinguished (cf. Lawicka & Konorski, 1961). Denotations as in Figure 13.3. (*a*) Block of 30 trials (2 experimental sessions) in which a preference for running to the left food tray is observed. (*b*) Two blocks of 30 trials each in which left food tray was not signaled; note that the number of errors to that food tray decreases. (*c*) Block of 30 trials in which again all food trays are signaled; note that the preference for running to the left food tray does not reappear.

preparatory stimulus either remains where he is, or, at the most, approaches some food tray only a few times, the prefrontal dog ran to various food trays again and again in many successive sham trials (see Figure 13.5). We adopted the rule that the sham trials were repeated until the animal did not go to any food tray on release, but remained on the platform. Only then was the following true trial with distraction given. But at the beginning of this training running to the food trays in sham trials was so persistent that we had to repeat them 15 times in succession and then, although their extinction was not achieved, a true trial was given. In view of so many sham trials being required after each true trial, in the first sessions of this series only five true trials were given; otherwise a session would last too long.

Figure 13.6 represents the mean number of sham trials with positive responses in each 15 trials. It is seen that gradually, although very slowly,

the reactions of approaching the food trays in the sham trials decreased and eventually dropped almost to zero.

In Figure 13.7 the distribution of the runs to various food trays in sham trials is shown. It is seen that the overwhelming majority of runs are to the left food tray, and only in the last block is this preference

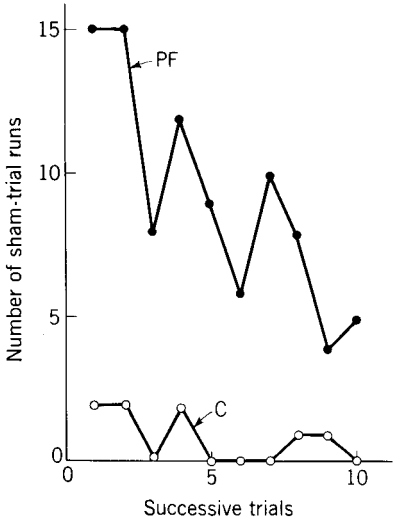

Figure 13.5. The number of responses in sham trials in prefrontal and control dog on 10 successive trials. Abscissa, successive true trials; ordinate, the number of responses in sham trials after a respective true trial. *PF*, the dog after ablation of the prefrontal area; *C*, a dog after ablation of the dorsal premotor area. (From experiments of I. Stepień.)

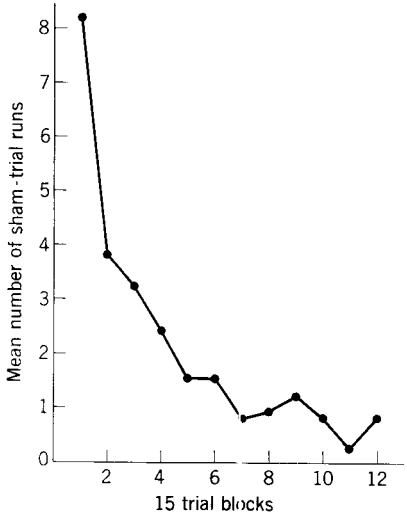

Figure 13.6. The mean number of responses in sham trials in each block of 15 true trials. Abscissa, successive blocks of 15 true trials each; ordinate, mean number of responses in sham trials per one true trial in each block.

no longer seen. It should, however, be noted that even in the period of the strongest preference of runs to the left food tray, in the sham trials following *immediately* the true trials the animal simply repeated the same run which was just reinforced; i.e., he made for the most part "last response errors."

What was the effect of the above procedure on the animal's performance in true trials with distractions?

As is seen in Figure 13.8 the effect was immediate and very prominent. The number of errors dropped significantly so that in some ses-

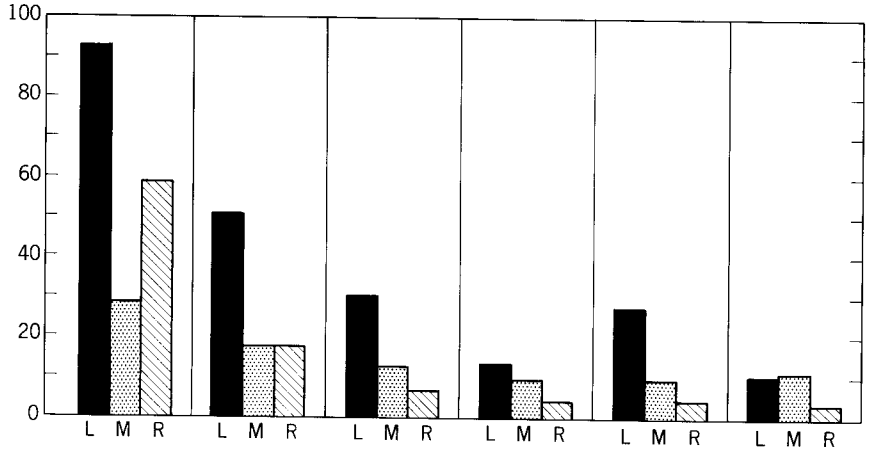

Figure 13.7. Distribution of runs to particular food trays in sham trials. Each block of bars denotes responses in sham trials after 30 true trials. *L,M,R* denote number of runs to the left, middle, and right food tray respectively. Note the high preference of running to the left food tray which subsides only in the last block.

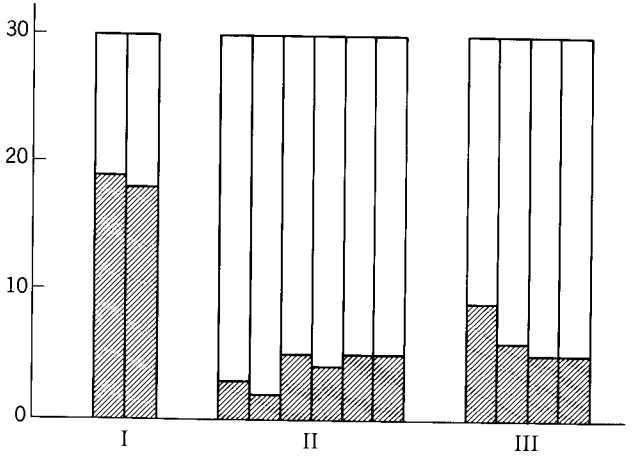

Figure 13.8. The effect of sham trials on the DR with distractions. Each bar denotes 30-trial block. I, number of errors in last experiments with distractions without sham trials. II, experiments with distractions in which sham trials were introduced. III, experiments with distractions after sham trials were withdrawn.

sions no errors were committed at all. When we returned to the original method of conducting experiments (without sham trials), the improvement appeared to be lasting. It is worthwhile to note that now the few errors committed by the animal were nearly always last response errors and no more preferential errors were made.

Discussion of Hypotheses

The experimental material presented in this paper, supported by analogous findings published elsewhere (Lawicka & Konorski, 1962, 1963) and by our earlier data obtained on cats (Lawicka & Konorski, 1961) allows us to draw the following conclusions concerning the character of the impairment on DR in prefrontal animals.

First, we have seen that even in most severe cases of DR impairment, as produced in trials with distractions, the correct response *is* obtainable whenever the appropriate experimental procedure is applied. This fact indicates that recent memory of directions is not abolished by the prefrontal lesions.

Secondly, we have much evidence to show that the majority of errors committed by the animals in the DR test have a perseverative character, reflecting specifically either a preference for approaching a particular food tray, or tendency to repeat the response made on the preceding trial.

The simplest hypothesis which would seem to account for these findings is that ablation of the prefrontal area, or rather some specific part of it, produces an increase of a perseverative tendency which blocks the correct DR performance. This hypothesis was proposed by other authors (Settlage et al., 1948; Mishkin et al., 1962) and was also put forward in our earlier papers (Lawicka & Konorski, 1961, 1962, 1963). It seems, however, that this hypothesis is untenable for the following reasons:

First in recent experiments performed by Lawicka (unpublished) it has been shown that, in an experimental situation quite similar to that described above, prefrontal dogs did not exhibit any perseverative tendency in a test which did not involve DR. The dogs were trained to go to the left or right food tray in response to two tones sounding from a loudspeaker located in front of the animal. The task appeared to be very difficult and the dogs mastered it only after a considerable number of trials. Nevertheless, prefrontal lesions did not produce any deficit in this test, nor did the animals display any perseverative tendency, even if the response to the same food tray was reinforced several times in succession. On the other hand, the data presented in Figure 13.9 show that the same animals were strongly impaired in DRs with distractions, and on the DR test they exhibited a strong perseverative tendency. It should be added that in normal animals the DRs with distractions are much easier than the go left–go right differentiation to nondirectional sound stimuli, and the performance of the former test is much better than that of the latter.

These data show that the perseverative tendency itself is not increased

after prefrontal ablations, and that in our experimental condition it is manifested only in DR tests.

By the way, it should be noticed that the above findings disprove the hypothesis put forward by Stanley & Jaynes (1949), according to which the impairment of DRs in prefrontal animals is due to the lack of inhibition of incongruent responses ("act disinhibition"), and another hypothesis

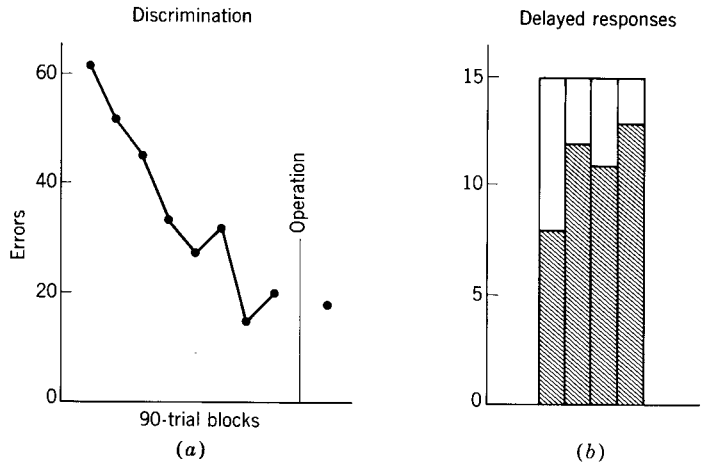

Figure 13.9. Comparison of the effect of prefrontal lesions on sound go left–go right discrimination and delayed responses. (*a*) Training of discrimination before operation, and its full preservation after operation. Abscissae, successive experimental sessions in 5 session (90 trials) blocks; ordinates, numbers of errors in each block. (*b*) Number of errors in the same dog after operation on delayed responses with distractions (Lawicka, unpublished experiments).

claiming that prefrontal animals exhibit an increased "positional habit" (cf. Mishkin et al., 1962). Indeed, neither "act disinhibition" nor increase of the positional responses is seen in the test just described in prefrontal animals.

Secondly, it should be emphasized that the perseverative tendency appears in normal subjects in all those cases in which the cue for the given response is not clear enough, as is the case in the first stages of discrimination training, or in unsolvable situations throughout the training ("hypothesis" of Krechevsky, 1932).

Thirdly, perseveration symptoms appear in abundance in human pathology after damage in various parts of the brain, and take different forms depending on the site of lesion. According to our observations made in the Neurosurgical Clinics of the Polish Academy of Sciences (unpublished experiments of Konorski and others) different forms of aphasia produce

perseveration in different types of responses. And so, patients suffering from the so-called "amnesic aphasia," display a strong perseveration in visuoverbal responses, i.e., in naming objects or pictures presented to them. On the other hand, patients suffering from "sensory aphasia," producing an impairment in the comprehension of speech, display equally strong perseveration especially in audiogestural responses, consisting of persistent and inappropriate responses in indicating objects after hearing their names, or fulfilling orders. The patients suffering from so-called "conductive (or central) aphasia," encountering great difficulties in repetition of the words heard, manifest a tendency to perseveration especially in audioverbal responses.

And so we see that after focal lesions of the brain producing impairment in different systems of reactions, the perseverative errors may be chiefly or exclusively found in that system which is impaired.

To sum up, we may conclude that we have hardly any evidence that the "increased perseverative tendency" represents a primary symptom produced by the brain lesion which is *responsible* for the given disorder either in learning of the given task or its performance. Rather the opposite seems to be true, namely, that the perseverative tendency appears as a secondary adjustment of the animal to a partially or totally unsolvable task presented to him. This may happen either when the given system of discriminative responses is not yet developed (or cannot be developed at all), or when it is impaired by an appropriate brain lesion.

If so, then we should look for an explanation of the poor performance of the DR test by prefrontal animals not in the increased perseveration, but rather in the impairment of some mechanisms intrinsically involved in the DR procedure. Two alternative hypotheses of such an impairment may be advanced.

According to the first hypothesis the essential factor producing the deficit in DR performance by prefrontal animals would be the weakening of the reflexogenic strength of the trace stimulus determining the direction of the animals' response after release. This hypothesis may be directly inferred from our above discussion of the origin of perseverative symptoms, in which we have stated that these symptoms are closely connected with the impairment, or poor development, of a given system of responses. Since, as we have seen, perseveration in prefrontal animals affects only those discriminative responses which are elicited by trace stimuli, the conclusion may be drawn that these stimuli do not provide sufficient cues determining the animals' response in the DR test, i.e., that their reflexogenic value is diminished.

It would be important, too, in this place to emphasize the essential

difference between the view proposed here and the old concept of impairment, or abolition, of the recent memory after prefrontal lesions. According to the latter concept the traces of the preparatory signal are more transient than in normal animals, i.e., the animal simply *forgets* sooner where he should go when released, and therefore reacts on the chance level or nearly so. According to our view the impairment of animals' responses has nothing to do with forgetting, since, as shown in our experiments, the correct response may occur after the same delay period as in normal animals. However, the trace of the preparatory signal is now weaker as the CS than it was before and cannot stand competition with other intervening stimuli.

Let us try, on the basis of this hypothesis, to explain the DR disorders found in our studies.

In the DR procedure the instrumental response (approaching the appropriate food tray) is elicited by a compound stimulus composed of (1) the trace of the preparatory stimulus, and (2) the actual stimulus of release. As well known from the Pavlovian studies on compound conditioned stimuli (Pavlov, 1940), the stronger component of the compound overshadows the weaker component so that the CR to the latter one (when it is applied alone) is much reduced, or even nonexistent. Now, we assume that in normal animals the trace CS left after the preparatory signal is as strong as, or even stronger than, the release stimulus, and therefore it can determine the animal's responses. And so, in normal trials the animal reacts in most cases correctly and in the sham trials (when only release stimulus is given) it does not react at all.

But when, owing to the prefrontal lesions, the reflexogenic strength of the trace stimulus is reduced, the actual release stimulus acquires the leading role and the trace stimulus is now overshadowed by it. But since the release stimulus cannot by itself determine the direction of the response, the animal is confronted with a partially unsolvable task and acts under a simple instrumental conditioning strategy by repeating those reactions which were recently, or most frequently, reinforced.

Our hypothesis allows us also to understand why the animal is able to improve his performance significantly when special measures, such as described above, are applied. To turn again to the Pavlovian studies on compound CSi, we know that when the stronger component of the compound is applied alone without reinforcement, while the whole compound continues to be presented with reinforcement, the stronger component loses its dominant character and the leading role is transferred to the weaker component.

It is easy to see that this is exactly what was done by introducing the sham trials: the releasing stimulus was applied alone without rein-

forcement so many times that it was completely extinguished, and in consequence the dominant role of the trace of the preparatory signal could be reestablished.

The hypothesis under consideration seems to account for many prefrontal symptoms in man, when the patient is not able to act under an instruction given beforehand, although he remembers it perfectly and can easily repeat it (cf. Luria, Chapter 17). It may be admitted that the instruction given beforehand is nothing but a trace CS analogous to those dealt with in our DR experiments. Since the reflexogenic value of this stimulus is now reduced, it is no longer sufficient for eliciting the proper response, especially when diverting actual stimuli are in operation.

On the other hand, the present hypothesis cannot obviously explain another major deficit of prefrontal animals concerning reversal learning (cf. Harlow & Dagnon, 1943; Settlage et al., 1956), since in this test we have to do exclusively with actual and not trace stimuli. It may be guessed that the process of reversal learning is more complex than usually thought, involving some sort of trace stimuli (such as general program of reversing), that it depends on another mechanism represented in other parts of the prefrontal area, or else that the hypothesis now under discussion should be rejected.

An alternative hypothesis which may account for our data refers not to the weakened reflexogenic value of trace CSi, as the chief factor in the DR deficit in prefrontal subjects, but rather to the increased reflexogenic value of actual stimuli.

There are many observations pointing out that animals after frontal lesions display an exaggerated orienting reaction toward the external stimuli. This property of the frontal animals was often referred to as hyperreactivity (cf. Rosvold & Mishkin, 1961) and was considered to be responsible for their increased "distractability." In dogs and cats these increased reactions were in fact observed by us, particularly when the source of the auditory stimulus was remote from the food trays. They were also observed in CR experiments after combined premotor and prefrontal ablations (Stepień et al., 1960). Generally speaking we can admit that the frontal animals (as well as humans) are more "stimulus bound" than normals. Perhaps one can explain this symptom by supposing that specific parts of the frontal region play a role in suppressing these reactions in the course of habituation, and that their ablation leads to "dishabituation."

Now, there is again some evidence showing that the orienting reaction toward a stimulus plays a positive role in the process of conditioning. In fact, stimuli producing stronger orienting reactions are more easily

conditioned than those producing weaker reactions, and the CRs established to them are more stable and resistant to extinction (Pavlov, 1940). In consequence one can admit that prefrontal animals are not less, but rather more prone to develop conditioned responses, and these responses may become more strong and resistant to extinction than those in normal animals.

This reasoning seems to explain satisfactorily our data concerning the DR deficit in prefrontal animals. In our experiments the DR is always preceded by the immediate stimulus provided by the releasing procedure. If the animal, after being released, goes to the proper food tray and receives food there, the bond between the releasing stimulus and the response may become stronger in the prefrontal animal than in the normal one, hence the increased tendency to repeat this response in the same condition. This is the source of perseverative errors observed so often in our prefrontal cats. After performing such an "unwanted" conditioned response the animal *is* able to go to the proper food tray, since the trace of the preparatory signal is totally preserved.

Since the perseverative responses are not reinforced by food they eventually become extinguished and in consequence the animal's DR performance is gradually improved.

The handicap of cats in comparison with dogs in the DR test is that they are usually not able to preserve their bodily orientation if the delay period amounts to 1 min, or so. Therefore, their performance in DRs without distractions is poorer than that of dogs. However, when in experiments with dogs distractions are introduced interfering with their bodily orientation, then their performance, as we have seen, is strongly deteriorated, but again this deterioration is based on the same principle. Now, presentation of food on the platform plus releasing stimulus become so strongly connected with the given reinforced response that the animal performs again and again this response instead of the correct ones, the more so because from time to time it is indeed reinforced. The strength of the bond established between the distractive stimulus and the response in the prefrontal animal is best proved by the exceedingly strong resistance to extinction of this response in sham trials, as compared with the normal animals (cf. Figure 13.5). However, when after many sham trials extinction is reached, we observe an immediate improvement in the animal's DR performance, showing again that his recent memory of the preparatory signal is not impaired.

The hypothesis presented here, in contradistinction to the previous one, allows us to account not only for the data described in this paper but also for the large body of evidence showing that, while the prefrontal animals are generally as good as the normal ones in original discriminative learning,

they are dramatically impaired in any reversal of discrimination, as shown long ago by Harlow's group. The difficulty in reversal learning would be simply explained by the abnormal strength of the conditioned connections established in the original training.

CONCLUSIONS

The chief aim of the present paper was to discuss various hypotheses concerning the disorder of the DR performance in prefrontal animals as revealed in our experiments on dogs and cats. It was shown that the concept of a deficit of recent memory being the essential factor of the DR impairment cannot be true, since according to our experimental evidence this deficit does not exist. The theory of act disinhibition also cannot be held since this sort of inhibition is not impaired even in much more difficult discrimination tests. It also seems that the impairment cannot be due to the increase of positional habits. It has been shown that increased perseverative tendency manifested by prefrontal animals in the DR test cannot be considered as the cause of the defect, since it does not appear in these animals in other discrimination tests, and does appear after nonfrontal lesions. It was suggested that perseveration is a secondary symptom related to the impairment, or poor development, of a given system of responses.

Two alternative hypotheses satisfactorily explaining DR disorders in prefrontal animals were discussed: one of them attributed these disorders to the decrease of reflexogenic strength of trace CSi, while the other one pointed to the increase of the reflexogenic strength of the external stimuli as the chief factor disturbing the DR. The latter hypothesis seems to cover not only the DR deficit but also the impairment of reversal learning observed in prefrontal animals, while the former does not.

It should be added that the two hypotheses presented here do not exclude each other, and it may be supposed that both the mechanisms discussed above can be jointly or separately in operation, depending on the exact localization and/or extent of cerebral lesion.

NOTE: The authors are greatly indebted to Dr. M. Mishkin and Dr. H. E. Rosvold for their valuable comments and suggestions in preparation of this paper.

DISCUSSION

DR. MISHKIN: I would like to ask some questions about your second alternative, *stimulus-bound behavior*. Isn't object discrimination reversal per-

haps the most favorable situation in which to find deficit on the basis of stimulus-bound behavior?

DR. KONORSKI: Yes.

DR. MISHKIN: And yet our evidence in monkeys suggests that animals with orbital lesions are impaired to a greater degree on object discrimination reversal than are the animals with lateral lesions which failed delayed response. Thus, it seems that anatomical-surgical procedures have dissociated stimulus-bound behavior from the mechanism underlying delayed-response defects. Stimulus-bound behavior cannot account for the lateral animals' greater loss on delayed response.

DR. KONORSKI: Yes. I agree with you, and I cannot find a good explanation except that maybe reversal training in object discrimination is much more complicated than we think, and not properly understood at present.

DR. TEUBER: Since I put this very seductive word "stimulus-bound behavior," into your mouth, Dr. Konorski, I want to say that I got it from Goldstein (1927, 1944). And like so many of Goldstein's concepts, it is a very beautiful, but also a rather global descriptive term; and I think the best thing we can do with it is now to see how we can perhaps take it apart a little further.

If Dr. Mishkin could show that his orbital animals are very bad on object alternation, yet do delayed response rather well, this would please me no end, because it would confirm a suspicion I have had a long time, that delayed response after all has something to do with postural mechanisms and that its defect is neither a memory defect nor a generalized form of being at the beck and call of whatever happens at the moment in the environment.

I recall a patient among our cases of gunshot wound of the frontal lobes who has in many ways what people would call a classical frontal lobe syndrome. He is boisterous, jocular, and impetuous. He is youthful looking, and probably will be so for decades. We can never tire him out in our tests. Here is one of his typical exploits: One summer he had been in a rest camp where he performed some unskilled work. His first job assignment was dishwasher in the camp kitchen, but he lost that job because he was rather clumsy and broke too many dishes. After that he was put to work in the garden where he was assigned to another man who was digging ditches; our patient had a big pair of shears with which he was to cut roots. Every time these roots appeared, he had to cut them so the other man could go on with his shovel. And while a ditch was opened, a huge thing appeared: four black strands lying side by side. The patient was standing there, and the subsequent episode was described by both the patient and by his companion. He said, "Ha ha, it's not a root. It looks like a root [going through the motions

of cutting]. It looks like a root. It's not a root. Why are the fire alarms ringing?" By cutting the strands he had shorted out all the cables that led to the fire alarms all over the camp.

He assures us that he did this because he couldn't help it. But he knew he shouldn't have done it. And when he makes mistakes on tests, this is precisely what he says, "I knew what I was supposed to do, but I couldn't help it." And yet, and this is the bad part of it, this man does so well on delayed-response and delayed-alternation tasks that his examiners have a great deal of trouble keeping up with him.

So again you have this apparent dissociation there.

DR. WARREN: I don't believe that the data from cats or dogs necessarily imply a close association between reversal and delayed-response losses because the cats show defects in discrimination reversal learning without being seriously impaired on delayed response. As far as dissociation is concerned, there is no argument.

DR. MEYER: There is only one way to describe this work: it has the simplicity of genius. No investigators prior to this had asked, of any frontal preparation, whether second choices would be better than the first, the ones that interested the rest of us. Now that we have seen the possibilities that this approach has introduced, I suspect that studies of the frontal syndrome never will be quite the same again.

The studies must certainly go on. While we can accept the points that have been made in this beautiful analysis, there is rather evidently much that still is not completely settled to our satisfaction. Therefore, it would seem to be worth our while to look at some of the remaining quandaries, and to look at how our past hypotheses have fared appears to be one way of doing it.

These hypotheses have seemed to me to fall within four fundamental groups. We can argue, first of all, that frontal monkeys show a deficit in the delayed response because they lack a necessary mechanism for the learning that must take place every trial. If this is the problem, there would seem to be but two important sources of the failure. The first is that the animal does not attend, but otherwise is like a normal monkey; the second is that it attends, but rapidly forgets, the problem being centered in fixation. These distraction and inaction concepts both have much to recommend them to us, but there is as yet no compelling proof that either is the principal factor.

The other major viewpoint is that frontal monkeys learn delayed responses like the normals, but that their performances are poor because of various kinds of interference. Such interference could be due to prior events,

and hence we would describe it as proaction; it could, on the other hand, develop afterward, and if so, we would term it retroaction.

Professor Konorski's hypothesis would be a form of the proaction concept, as is the Settlage-Zable-Harlow point of view and that of Rosvold, Brush, and Mishkin. I believe that there can be no quarrel with the point; such effects most certainly exist. However, I believe that it is doubtful that proaction of whatever kind can be considered to be fundamental to the deficits observed in Jacobsenian delayed response. In this I agree with Dr. Mishkin, but my conviction is an old one. One reason is that we performed experiments of the approach-aversion sort in the Harlow-Davis-Settlage-Meyer study that appeared in 1952. We observed the Brush-Mishkin-Rosvold effect, but didn't explore it in detail; it was there, but nonetheless was so slight that it seemed impossible that deficit in the delayed response could have its source in such a variable.

Retroaction has been little studied. The one experiment that comes to mind at once is, of course, the Malmo study, and I think that it suggests that retroaction has to be considered. It is more important, though, in my opinion, that he used the indirect method, and that his experiment is thus more similar to this one than the usual monkey study. The reason why we have so few retroaction studies is that, with direct testing methods, frontal monkeys are so poor that added retroaction could not possibly have made them worse. We can nonetheless suspect that retroaction, in itself, is not too consequential, and the evidence for this, I think, comes from discrimination studies. Frontal monkeys can be trained to do extremely well in two-trial discrimination problems, albeit not so well as animals with no operations whatsoever. When a frontal monkey picks an object and is then reinforced or not, something happens which is very durable as measured by performance on a single, second trial. Nothing happens, seemingly, when one drops a peanut under one of these same objects and, as quickly as it can be done with trays, presents the frontal monkey with a choice. His performance, generally, is very little better than chance, and it is about as good with minimal as with long delay.

I have thus a firm belief that the deficit is basically a learning deficit. Whether distraction or inaction is the answer certainly is not at all clear, and if inaction is the revelant concept, there are many facets to explore. Finan's old experiments along these lines continue to strike me as impressive, as does the Campbell-Harlow reasoning if not the Campbell-Harlow results.

In how many ways can a discrimination trial differ from setting for delay? If we think in terms of two-trial problems for the discrimination

case, the number of alternatives is clearly small enough that each and every one can be explored. First, we need to understand the nature of the difference between direct and indirect methods, for the latter seems to yield performances without the giving of a food reward. Stimulus stability is possibly the answer, as we suggested long ago, and it is an issue that can be resolved only through improvements in our instrument. One approach, which we are now pursuing, is to give control of presentations to the monkey so that, in effect, the instability is limited to that which he produces. We are hoping that the basic format, which permits of many variations, can be used to settle the remaining issues in a parametric manner.

DR. KONORSKI: Let me explain more precisely what I mean by greater or lesser reflexogenic strength of trace CSi, and why these terms have nothing to do with stronger or weaker recent memory.

By using our triple-choice method of DRs the following variety of experiments could be performed: While the animal is on the leash, we apply not a single preparatory signal, but two of them one after another, i.e., either two buzzers, or two lights from two different food trays. After release, the animal [I am speaking here only of normal animals, since the prefrontals are severely incapacitated in this test (cf. Lawicka & Konorski, 1962a)] runs, as a rule, to the food tray signaled by the second stimulus and, after having eaten food there, he immediately runs to the other one. However, if we apply two different signals, namely, first the buzzer from one food tray, and then the light from another one, the animal usually goes to the food tray signaled by the buzzer, and then only to that signaled by the light. This is because the reflexogenic strength of light (and its trace) is weaker than that of the buzzer; this, however, does not mean that the animal does not remember wherefrom the light was operating, since the animal unmistakably goes to the food tray signaled by it, in spite of heavy distractions brought about by going to the first food tray and eating food.

In other words, the stronger reflexogenic value of one stimulus over another means that in competition between them the priority of response is given to it and the response to the other one may be even totally blocked.

DR. SUBCZYNSKI: Perhaps, the role of "stimulus binding" in prefrontal lesions becomes more evident in the following tests which we performed on human patients with prefrontal lobotomy. We used two tests.

The first one was simply counting 1, 2, 3, and so on; then the more difficult counting of odd numbers, 1, 3, 5, 7, and so on was required. As you would expect, frontal patients could handle such simple problems where shifting was required in respect to only one element. However, in the second test, two and even three elements had to be shifted simultaneously. For example, like this: $1 + 2 = 3$; $3 + 4 = 7$; $7 + 6 = 13$; and so on.

This problem is pretty difficult to solve for the patients with lesions of the prefrontal lobe because of their tendency to perseverate. Now this is not suprising, as this phenomenon is well known. However, we found an additional feature: while the prefrontal patients fail to solve these problems in their heads they are able to solve them if they are allowed to use pencil and paper. Yet, even if the same patient had performed the task four to five times on paper, they could not repeat it in their heads. Thus, it seems that they need the actual stimulus and fail to utilize response traces. This seems in agreement with Dr. Konorski's first theory according to which the response traces decay so rapidly after injury to the frontal association cortex that problem solving is dependent upon support from the external environment.

DR. AKERT: I would like to ask Dr. Mishkin whether it is perhaps possible that the difficulty in spatial learning by the lateral animals is in any way connected with the removal of area 8, that is, the anterior bank of the arcuate sulcus. The lesions in your recent group of animals called "dorsolaterals" do include area 8. The reason I am asking this question is that from the material I saw in Dr. Nauta's laboratory, it seems that the area of the thalamus which projects essentially on area 8, the paralamellar portion of medialis dorsalis receives afferents from the cerebellum, and also probably from globus pallidus. In this respect, the paralamellar portion of medialis dorsalis resembles nucleus ventralis lateralis, which projects upon precentral motor cortex. Now, area 8 is a motor area, controlling to some degree eye and head movement and perhaps the axial musculature. Yet, in some other respect it belongs to the frontal granular cortex. Perhaps we should separate area 8 sharply from the rest of the lateral frontal response system, as well as from the agranular frontal cortex.

DR. MISHKIN: I think this is a possibility. There is evidence against it, but it is probably not critical; that is, area 8 lesions by themselves do not produce defects in spatial alternation learning, while lesions of the principal sulcus by itself do produce impairment on spatial alternation. So it would seem as though it is the area around the principal sulcus that would be most important. But this is not to say that there isn't a combination of defects, perservative and spatial, due to a combination of lesions on the lateral surface which combine to produce the severe defect in spatial alternation that we get. I don't know the answer to that.

DR. THOMPSON: If we examine the difference between simple visual discrimination reversal versus a spatial discrimination reversal, everything else being equal, we have two problems differing largely in terms of the modalities involved in mediating these reversal habits. But are they really equal in respects other than the modality?

For example, visual discrimination reversal may be more difficult than

place reversal, in the sense that the difference between spatial cues, between left and right, would be greater than the difference between the two visual stimuli. And therefore, since you did not run them to criterion, and since you gave them a limited number of trials, it is not surprising that the animals failed to reach the same level of performance on the two tasks prior to reversals. Much recent data show that overlearning the original habit facilitates reversal performance. The reversal experience is more vivid when you have 50 trials in a row followed by reversal as opposed to three.

The other difficulty: Even though you have two different problems on which animals may achieve the same level of performance the neural mechanisms involved may differ in complexity. This can be shown by their differential sensitivity to convulsive shock. Simple position reversal is not affected by convulsive shock. Apparently the response patterns are consolidated in the brain immediately. In contrast, more complex visual pattern discrimination habits are severely affected by electroconvulsive treatment.

In conclusion then, differences in behaviorally defined habit flexibility and neurally defined trace systems formed as a result of a comparable amount of training may be responsible for the apparent differences in visual and spatial problem solving by orbital and lateral monkeys. These factors should be isolated experimentally. The visual versus spatial contrast is oversimplified.

DR. TEUBER: I want to point out that I think there are quite a number of positive points in our perplexing discussion. I think the tremendous virtue of this monkey wrench that Dr. Mishkin has so skillfully inserted into our conception of the frontal lobes is simply that he pushes us very hard toward at least a two-factor theory.

I think no matter what our theoretical conception might have been about a behavior change that could account for a variety of symptoms, no matter whether we have managed logically to reduce a number of symptoms to one root symptom, if somebody comes and shows us two symptoms that are clearly dissociable by different lesions, then he has shown that the ablation method adds information not obtained by the behavioral analysis alone. That is why all of us are committed to working from both ends—from the behavioral analysis and from the anatomical analysis—and to bringing them together.

Many years ago, Lashley made the suggestion implied in your comment, Dr. Akert, that delayed-response defects were produced by oculomotor discoordination (Lashley, 1950). This idea was very promptly refuted by demonstration that the essential lesion for delayed-response deficit is simply not coextensive with the frontal area from which you get the best oculomotor effects. But I think we should reflect further on the nature of these oculo-

motor effects that one gets from lateral and dorsal lateral frontal regions; these areas are of course much more extensive than the so-called area 8. They are not simply impulses to turn the eyes one way or the other, but very complex compensatory effects, as you undoubtedly know. And maybe there is more to it. I think that proper analysis of the lateral frontal monkeys' disturbed behavior might tell us something about the way in which oculomotor functions are normally used in preparing an animal for an ensuing sensory change so that sensation is not disturbed by motion (Teuber, 1960).

I also think that the alternation tasks and the spatial reversal tasks might depend on an adequate perception of relationship between the animal's own body and the environment. At the very end of my own talk I will show some rather strange data in which frontal patients have trouble on a test requiring proper orientation toward their own body—a task that used to be considered of special diagnostic value for the parietal lobe syndrome. Yet it is apparently vulnerable to frontal lobe lesions.

I think we might come to terms with delayed-response deficit yet. It has only been around for 30 years now, and we should give it time. We can't do it in three days.

DR. KONORSKI: Yes, I agree. Considerable progress has been made in various laboratories recently, and we have come to grips with new problems during this symposium. The paradoxical situation created by the experiments of Mishkin has helped us to discard older hypotheses and given us new problems to be resolved. I think some of the problems raised during the discussion clearly indicate one thing: we need more data before further progress in understanding the several functions can be made.

Concerning the two possibilities which I put forward tonight, I think that possibly both of them may prove to be correct in interpreting situations which may depend on different lesions. As far as the stimulus-bound behavior is concerned let me give you another line of evidence which occurs to me just now. Not long ago, Hernandez-Peon and coworkers (personal communication) found that stimulation in the septal area produces a symptom in cat which they called the "magnetic orienting reaction." Such an animal has an exaggerated orienting reaction to some objects to which no attention was paid before. The cat looks at them fixedly for several minutes. This may reflect a primitive stage of the orienting reaction upon which a higher level of organization such as frontal cortex is superimposed.

The higher level of control would tend to inhibit the orienting reaction in order to allow attention to be shifted, to be increased or decreased depending on the significance of the stimulus. Perhaps, then, all these habits which are produced by extinction of orienting reactions may be partially due to

some processes which are going on in the prefrontal area. And hence, it is logical to assume that when the prefrontal area is removed, the more primitive mechanism of attention or orienting reaction is released. Perhaps this release of orienting reaction is a factor contributing to the delayed-response deficit among other things. This would add another aspect to the complex neural basis of the stimulus-bound concept mentioned tonight.