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THE PHYSIOLOGICAL MECHANISM OF PERSEVERATION

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ACCORDING to the generally accepted definition, we denote by "perseveration" any response, or as far as human beings are concerned, any image, which after a single or multiple elicitation becomes pathologically fixated, appearing to irrelevant stimuli, and being resistant to extinction. "Stereotypy" and "obsession" are other terms denoting these phenomena.

The perseveration symptoms are predominantly encountered in various pathological states, but occasionally they are also observed in normal subjects, particularly in children. In man, they occur most frequently in neuroses (e.g. in obsessional neuroses), in schizophrenia, and in many forms of organic brain disorders. They have also been described in animals after cerebral lesions. However, in spite of their relatively widespread and frequent occurrence, the pathogeny of perseveration has never been thoroughly analysed, and no attempts were made to clarify its physiological mechanism.

In the present paper, a number of typical examples of perseverative responses are reported, both in animals and man, and we wish to discuss their intimate nature, and the factors associated with their occurrence.

Perseveration in Experimental Neuroses

First of all, we shall turn to the consideration of perseverative symptoms observed in functional disorders of the nervous system. Pavlov and his co-workers were the first to show the perseveration syndrome in dogs, in the course of experimental neuroses. A typical example is the Filaretov's experiment, in which the dog was conditioned to a sound, produced by an apparatus situated under the Pavlov frame on which the dog was standing. In the course of these experiments, the intensity of the sound was gradually decreased, till it became nearly inaudible. It was found that the dog developed a sort of motor stereotype, consisting of drooping the head over the edge of the frame, and resembling a listening type of behaviour. This kind of stereotype response became so much fixated that it appeared persistently,

in spite of the fact that the stimulus was no more applied at all. Pavlov considered this type of phenomena as due to "pathological inertia" of excitatory processes, and incorporated clinical symptoms of obsessive neurosis and paranoia into the same category of neurotic disorders.

Similar disturbances in motor behaviour were often noticed in our laboratory, in particular in experiments dealing with type II conditioned reflexes. Fonberg (1953) described a severe perseveration syndrome, consisting of repeated flexion of the right foreleg, previously trained as instrumental in food responses. The perseverative response was here produced under conflict conditions. An interesting case of perseveration was reported by Maier (1949) in his experiments on rats. The author used Lashley's jumping apparatus, and confronted the animals with an insoluble visual discrimination task. It turned out that the majority of animals developed a habit of jumping to one door only, and this response became strongly fixated, and resistant to extinction.

There are many perseverative symptoms observed in the course of neurotic conditions in humans, and they have a similar character.

Perseveration After Frontal Lesions

We shall now turn to a different kind of experiments in which perseverative symptoms were occasionally present in normal subjects, and which were increased after frontal cortical lesions.

The work by Łukaszewska (1962) has been concerned with the problem whether or not rats are able to return spontaneously (i.e. without learning) to a starting place they left in order to grasp the food. An elevated T-maze

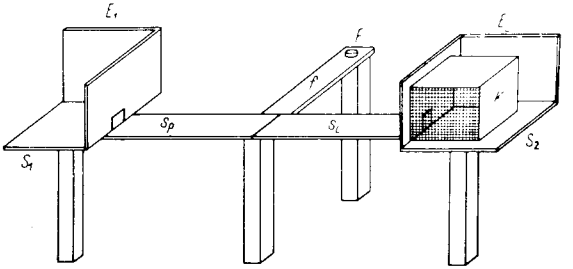

FIG. 1. A T-maze for experiments on return reaction. S_p, S_L—the arms of the maze; f—the trunk of the maze; F—place for food; S_1, S_2—starting platforms; K—cage.

was used, in which a screened cage was situated at the end of one of the maze arms, and a piece of biscuit was placed in the open space on the end of the trunk. The animals were required to leave the cage, run for the food, and grasp it, and then return to the cage where they ate the food. Since in various trials the cage was situated either in the left, or in the right arm of the maze, the rats, on their way back, had to remember from which place they had started for the food.

It has been shown that the rats were, in principle, able to solve this task correctly. However, in those cases in which, after a few runs from one side,

the cage was transferred to the opposite arm of the maze, the rats occasionally committed perseverative errors on their return, i.e. they made the same bodily turn as they did in the preceding trials (Łukaszewska, 1962). Such perseverative responses, being moderate in normal rats, were greatly increased after frontal lesions (Łukaszewska, unpublished).

In another experimental series, performed on dogs and cats by Ławicka (1959), the study of delayed responses and their properties, both in normal and in brain operated animals, was undertaken. Experiments were carried out in a rectangle with a starting platform situated in the middle of one wall, and the three foodtrays located at other walls. On each foodtray a buzzer was placed. The animal was fastened at the starting platform, and a buzzer on one of the foodtrays was put into action for 3 sec. This was a preparatory signal, determining in which foodtray the food was presented, after the animal has been released. When the animals learned to approach a signalled foodtray, during the sound of the buzzer or immediately after, the delay period, between the signal and the release of the animal, was gradually prolonged.

Experiments performed on dogs have shown that the animals are amazingly efficient in solving this test, even if the delay period lasted for several minutes or longer. The cats were generally less successful, but, in most instances, they were able to react properly after a 3 min delay period. However, from time to time it happened that they committed errors, consisting in running to the foodtray from which they had received food in the preceding trial (Ławicka, 1959).

It was found that after a removal of the prefrontal areas, the performance of delayed responses was dramatically impaired, both in dogs and cats. Analysis of errors has shown that most of them had a clear perseverative character (Ławicka and Konorski, 1961; Ławicka, unpublished work). Two types of such errors could be distinguished: in some cases, the animals after being released, approached that foodtray from which they received food previously; in other cases, the animals exhibited a strong preference for running repeatedly to one and the same foodtray. Since, after a false run, the animals often corrected themselves immediately and went to the foodtray indicated by the preparatory signal, it was concluded that the errors were not caused by any loss of the memory traces of that signal. It should also be emphasized that in zero-delay trials, the response was always correct and no perseverative errors occurred.

A similar tendency to a perseverative type of performance was observed in delayed response tests in prefrontal monkeys (Settlage *et al.*, 1948, 1956; Orbach and Fischer, 1959). There are also many clinical observations showing that a perseveration syndrome, consisting of performing repeatedly a motor act irrelevant to the given situation, often occurs in frontal patients. For instance, Teuber (1962) reported that a subject with a left frontal lesion was ordered to cut out roots of a tree in a garden; he then cut, with the same zeal, an electrical cable running under the ground, although he remembered the instruction, and knew that he was not supposed to do this. A typical test revealing perseveration in frontal patients consists in alternately drawing two geometrical figures, e.g. a circle and a square. After

a few correct responses (which show that the instruction was understood), the patient begins to draw repeatedly only one of those figures (Luria, 1962).

Another test, exhibiting the perseverative tendency in frontal patients, was devised by Subczyński (1961). The subject was asked to perform, in his head, some complex arithmetical operation, which necessitated to keep in mind two or three rules to be alternately obeyed, e.g. in such sequence as: $1+2=3$, $3+3=6$, $6+4=10$, $10+5=15$, etc. It was found that frontal

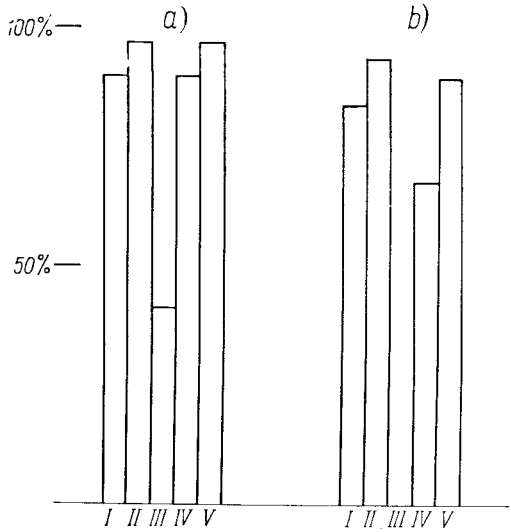

FIG. 2. Percentage of the correct responses in normal (a) and frontal (b) rats. I, II, III, IV, V—successive trials. Before the third trial the cage was transferred from one side of the maze to the other.

patients were not able to perform such tasks, because of a failure to switch from one rule to the other, and a tendency to hold only one rule, e.g. to add always the same number.

As seen from these examples, the perseverative tendency is so prominent and constant in frontal animals and patients, that some authors consider this symptom to be principally associated with frontal lesions. In fact,

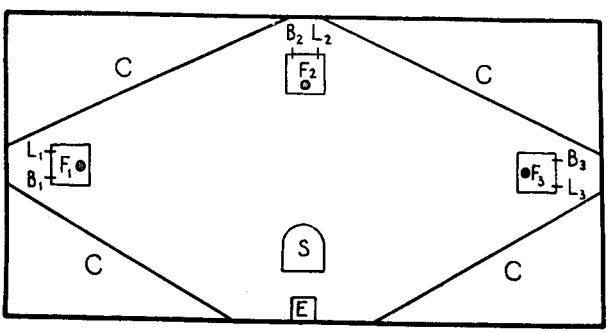

FIG. 3. The experimental situation for tests with delayed responses. *S*—the starting platform; F_1, F_2, F_3—the foodtrays; B_1, B_2, B_3—buzzers; *E*—site of the experimenter.

in some patients with prefrontal lesions, no other symptoms were seen. From this point of view, perseveration occurring in normal rats and also in children, might be regarded as a sign of poor development of frontal areas, either in phylogeny or ontogeny. Such an opinion, however, is erroneous, as evidenced by the fact that perseverative symptoms are produced not only by prefrontal lesions, but also by those localized within other parts of the brain. In fact, there are many observations showing that in speech disorders produced by the damage of temporal or occipital areas of the dominant hemisphere in man, perseverative symptoms are very conspicuous.

Perseveration in Aphasic Patients

In recent years, in the course of a study of aphasia (undertaken in co-operation with Stępień, Mempel, Srebrzyńska and Żarski), we have directed special attention to perseverative symptoms occurring in the verbal behaviour of patients. We have found that when examining aphasic patients by means of standard tests on repetition, nomination and comprehension, it is very easy to provoke perseverative responses, particularly when the

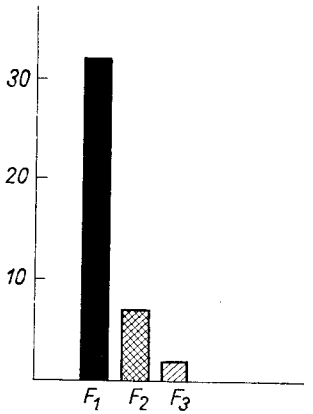

FIG. 4. Perseverative errors in delayed responses one day after prefrontal ablation. Columns denote the number of wrong responses to each foodtray. It may be seen that the animal has preference to approaching F_1.

trials follow quickly one after another. By performing such experiments, it was established that perseverative errors did not occur in all the patients, but only in those whose performance was impaired by an aphasia.

To illustrate this we present fragments of some protocols of relevant examinations.

1. A 59-year old patient, with a tumour of left temporal area, diagnosed on the basis of EEG, X-rays, and the clinical symptoms. Examination of his speech revealed marked defects, with no signs of impairment in naming, repetition and comprehension. Testing was done in quick succession.

Visuo-verbal responses (nomination):

The object shown:	Verbal response:
mirror	mirror
watch	mirror
spoon	mirror
fork	no answer
	Interval (of a few minutes):
soap	soap
comb	soap
pencil	soap
knife	no answer

In the tests of comprehension, the perseverative response occurred less often, and in those on repetition they were totally absent.

2. A 31-year old patient, with a surgically demonstrated tumour of the inferior-posterior part of the temporal lobe. Post-operative examination of speech revealed severe disorders in comprehension and also naming defects, without impairement of repetition.

Responses to spoken commands (comprehension):

Order:	The act performed:
close the eyes	closing the eyes
open the mouth	closing the eyes
give your hand	closing the eyes
	Interval of a few minutes:
show the watch	shows the watch
show the pen	shows the watch
show the matches	closes the eyes and shows the watch

There was also a tendency to perseveration in naming, but not in repetition.

3. A 39-year old patient, with a surgically confirmed tumour of the first temporal gyrus (Koźniewska, 1955). Examination of speech revealed considerable disorders of repetition, while spontaneous speech and comprehension were less impaired.

Repetition of speech (repetition):

Words heard	Verbal responses
goose, shirt	goose, goose
bee, coat	bee, bee
bird, children	bird, bird
fox, boy	fox, box, boy

In the tests, dealing with naming and comprehension, perseveration was not observed.

To summarize the results obtained in our examinations, we may say that we have established that perseveration in visuo-verbal responses was particularly evident in cases of amnestic aphasia; perseveration of audio-gestural responses occurred predominantly in sensory aphasia, while in "central" aphasia perseveration was characteristic for audio-verbal responses.

Discussion

Although our survey of perseverative symptoms is far from being complete, it appears to be sufficient for an analysis of their nature.

A subject, whether a brain-damaged patient submitted to a certain test, or an experimental animal, is required to react to a number of successively presented stimuli in a range of a given system of responses. And so, a dog or a cat, subjected to a delayed response test, has to react to the traces of

preparatory signals; similarly, a patient subjected to tests, concerning aphasia, has to name the object shown, perform the orders heard, or repeat the words, to which he was listening. In all subjects examined with our tests, we could establish that irrespective of the type of the brain lesion, the reaction to the given stimuli was generally adequate. This was clearly seen during the first trials of a given session. Only in the subsequent trials did the perseverative errors occur, consisting in repetition of one of the previous responses. It may be concluded, therefore, that perseverative errors occur because the traces of previous responses interfere with the proper response, and prevent its execution.

This result may be tentatively explained in either of the following ways. On the one hand, we may suppose that under certain pathological conditions, the traces of the reaction performed are abnormally fixated, resulting in a difficulty of switching to an alternative response. On the other hand, we may assume that a certain cerebral lesion impairs a given system of conditioned connections. Consequently, the reflexogenic power of a stimulus is too weak to overcome the traces of the preceding response.

It seems that in various nervous disorders the perseveration syndrome is produced by either of the two factors. We now have at hand good evidence that in functional disorders of the nervous activity the former of these mechanisms is in operation. In fact, we know that conditioned connections, formed under a very strong emotional stress (e.g. by a conflict), tend to become highly fixated, and may give rise to perseverative phenomena. Probably, this very mechanism is in operation both in the cases of experimental neuroses described above, and in obsessional states in man. It must be recalled that this mechanism of perseverative symptoms was anticipated by Pavlov.

It seems, however, that this explanation does not hold in all cases in which perseverative errors occur, e.g. in aphasia. It is, therefore, reasonable to suppose that in aphasia the second factor is in operation, namely that which is related to the impairment of conditioned connections within the given system of responses.

According to our concept concerning speech disorders of cerebral origin (Konorski, 1961), the difference between various types of aphasia consists in the differential impairment of definite pathways connecting various cortical areas engaged in speech function. Accordingly, we assume that the visuo-verbal responses which may be considered as a prototype of speech, are based on the integrity of pathways connecting the visual analyser with the motor analyser of speech. If these pathways are damaged, symptoms of amnesic aphasia follow. Similarly, the integrity of the pathways connecting that part of the auditory analyser which is concerned with the auditory analysis of speec hwith the visual analyser, is responsible for comprehension, and the pathways between the auditory analyser of speech and the motor analyser of speech is responsible for repetition. A damage to these pathways produces the so-called sensory aphasia, or central aphasia, respectively.

Let us analyse the behaviour of a patient suffering from amnestic aphasia during the visuo-verbal test. As seen from our examinations, the aphasic patient is able to succeed at first, thus showing that the association

between the visual image and the respective word is not lost. However, when, after a short interval, another object is presented, he tends to perseverate with the previous name, because the messages running through the affected pathways are too weak to overcome the existing traces of the previous excitation in the motor speech area. Only after a long interval, when the traces of the previous excitation have diminished, does the proper verbal response to the next stimulus become possible.

We shall now pass to a consideration of the mechanism of perseverative symptoms, occurring after prefrontal lesions (Konorski and Ławicka, 1963).

In spite of abundant experimental evidence, we are not able to decide which of the above discussed mechanisms is involved in the perseveration syndrome in prefrontal cases. On the one hand, it is known that prefrontal lesions in animals produce an increase in orientation reactions (release phenomenon), which may in turn greatly facilitate the fixation of conditioned reflexes, and make them more resistant to suppression. It is, therefore, very likely that the frontal rats in Łukaszewska's (1962) experiments, after having returned several times in succession along the same route, fixate this habit so strongly that it cannot be overcome by a change of position of the starting cage. Similarly, in the delayed response tests in Ławicka's (1959) experiments, the reinforcement of a run to a particular foodtray results in an increased fixation of this run, which is not to be suppressed in subsequent trials. The same explanation may be applied in discussing Teuber's (1962) case, in which the prefrontal patient severed the underground cable after having repeatedly cut roots of a tree.

However, all these phenomena may be also explained by supposing that the chief defect, following prefrontal lesion, consists in weakening the reflexogenic value of trace stimuli. In fact, all these cases in which the subject has to react to an actual stimulus, the response is always correct, and no perseveration is observed. However, when the response is determined by a stimulus applied well in advance, as in the case of delayed response test, or in all human tests based on instruction given beforehand, the subject fails to react properly, and tends to perseverate previous responses.

Only future investigations will elucidate which of these two mechanisms, or maybe both, are in operation after prefrontal lesions in man and animals.

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